

THE SURVEILLANCE PROGRAM

1964 - 1970

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**NAVAL MEDICAL RESEARCH UNIT NO. 4
GREAT LAKES, ILLINOIS**

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By

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From Naval Medical Research Unit No. 4 (NAMRU-4), Great Lakes, Illinois. This investigation was done in connection with Research Project No. MF 12.524.009-4013BE6I, Bureau of Medicine and Surgery, Navy Department, Washington, D. C. The opinions and assertions contained herein are those of the authors and are not to be construed as official or as reflecting the views of the Navy Department or the Naval Service at large. The experiments reported herein were conducted according to the principles enunciated in "Guide for Laboratory Facilities and Care" prepared by the Committee on the Guide for Laboratory Animal Resources, National Academy of Sciences-National Research Council. The animal care facilities are fully accredited by the American Association for Accreditation of Laboratory Animal Care.

THE SURVEILLANCE PROGRAM

High rates of recruit respiratory illness at Great Lakes observed over a 4-year period resulted in an average annual loss of approximately 29,000 man-days in training, and hospitalization costs estimated at \$900,000 per year. The incidence of acute respiratory disease (ARD) in military populations has been observed to be consistently higher among recruits than "seasoned" personnel. Careful descriptive studies of this phenomenon have been made only in the last few decades and demonstrated an epidemiological pattern which appeared to be specifically related to recruit training. The Navy recruit represents less than five percent of the entire Navy population, yet nearly 50 percent of all ARD occurs in that portion of the population.

In 1964, a continuous surveillance program was initiated to attempt to "fill in" missing pieces of that epidemiological pattern. The purpose was to identify etiologic agents responsible for respiratory diseases, their incidence and prevalence, and the morbidity and mortality associated with them. This study also covered inapparent infection by isolations from "well" individuals and serological response to agents in the population, thereby assisting in the definition of morbidity, infectivity, and virulence of the organism.

ARD admission rates of recruits at Great Lakes have repeatedly shown a characteristic winter high and summer low pattern since 1949 (Fig. 1). Epidemics of specific etiology still can be recognized as isolated events; for example, the streptococcal outbreak of 1955 and the Asian influenza epidemic of 1957. Since 1957, there has been an extended period of disease primarily due to adenovirus. The maximum incidence of disease appears between the second and third week of training, with 90 percent of all ARD occurring in the first half of training. This pattern remains so constant throughout the training periods that it has been designated the "finger-print" of ARD (Fig. 2).

The distribution of the incidence of hospital admissions for ARD with respect to time in training appears to be independent of the prevalence of ARD in the population; no reason for this phenomenon has been established. This pattern is apparent during severe epidemics as well as during inter-epidemic periods. The incidence of hospitalization for other conditions frequently forms a similar pattern. These observations suggest that stresses associated with recruit training may be an important factor influencing hospitalization rates.

"Rack passes" have been issued in lieu of hospitalization for cases of ARD. This has permitted the patient to return to his barracks for bed rest, generally for 24 to 48 hours, resulting in a decrease in admission for ARD. The incidence of rack passes and hospitalization for ARD complaints from January 1969 through May 1970 is shown in Figure 3. From January through March, the proportion of men receiving barracks bed

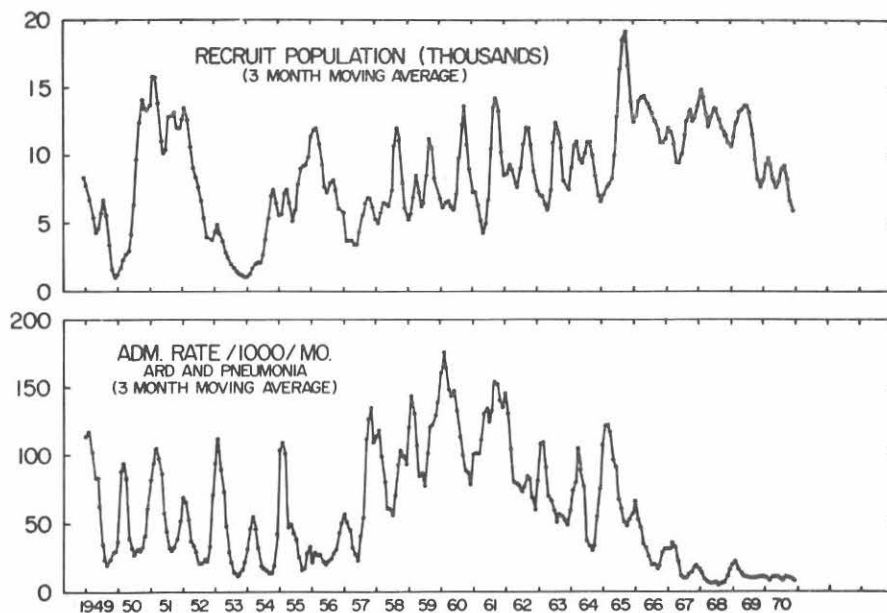


Fig. 1. Recruit population statistics and pneumonia admission rates, Great Lakes, 1949 - 1970.

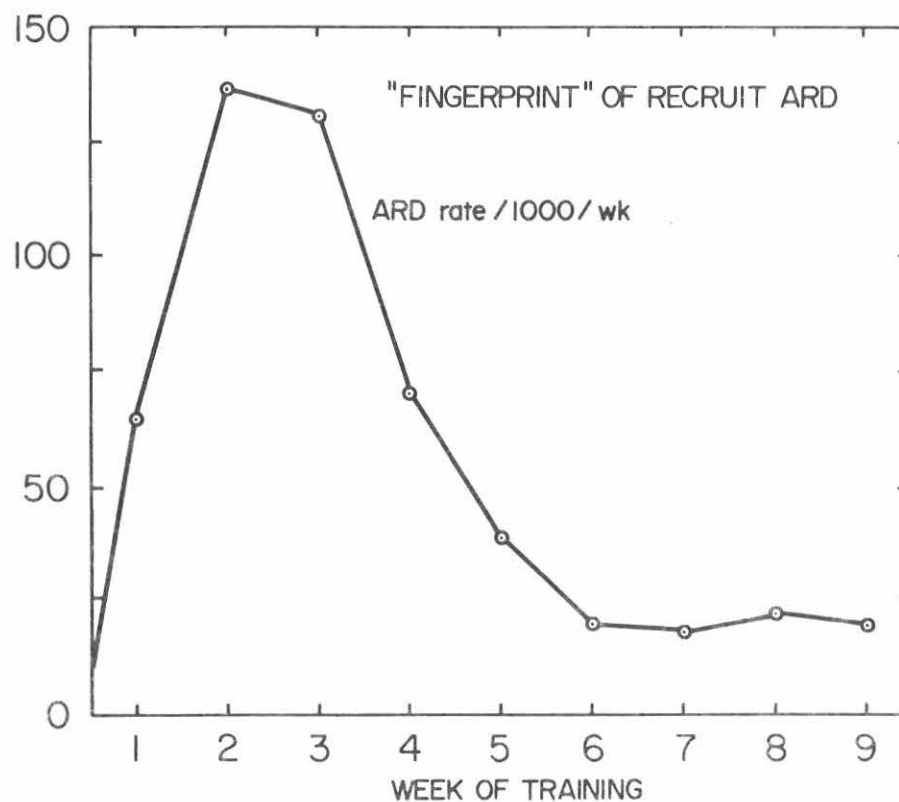


Fig. 2. The "Fingerprint" of recruit ARD.

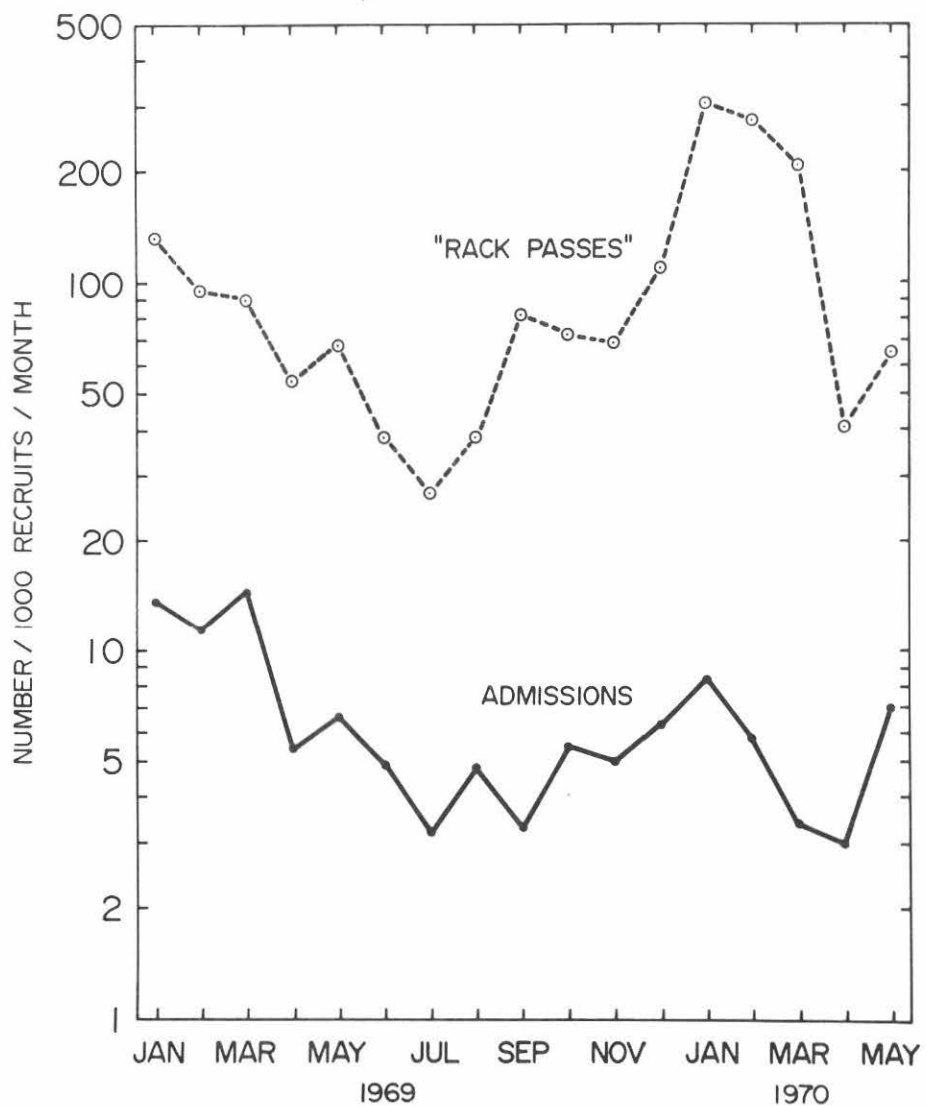


Fig. 3. The relationship of "Rack Passes" (limited bed rest in the barracks) to hospital admissions for ARD, Great Lakes.

rest for ARD had increased approximately from 10 to 50-fold the number of men admitted to the hospital.

Studies on ARD admissions have shown marked differences between cohorts of companies. The reasons for these variations in the incidence of disease are obscure. For a recruit to become a disease statistic, he must seek treatment at the medical facility; therefore, the factors which motivate the individual to seek treatment for his ailment dictate the incidence rates of disease. Barrack surveys have indicated less variance in the total disease experience than that reported at medical facilities. These observations complicate the epidemiology of ARD in military recruits.

Recruit Populations

The recruit population at the Naval Training Center (NTC), Great Lakes, Illinois is made up of young adult males, predominantly 17 to 20 years of age, who originate principally from the eastern half of the United States and, since October, 1968, principally from the northern two-thirds of the eastern half of the United States. A Naval Training Center at Orlando, Florida was commissioned in October, 1968 and young men from the southern one-half of the eastern half of the United States are now sent there. Another Naval Training Center is located at San Diego, California, which receives men primarily from the western United States. Men arrive continuously at the training centers for a 9-week training period. This provides continuous input of susceptibles into a central processing area where they are exposed to each other's infectious agents. In addition, there is exposure to any infectious agent currently prevalent in recruits already in training.

Companies are formed as the recruits arrive at the training center. About 3 days are required to administratively process, classify, examine, begin inoculations, and outfit a recruit. Approximately ten percent of the recruits are delayed in the processing area for various administrative or medical reasons. All recruits in processing are housed in the same facilities. After processing, the training company, composed of approximately 80 men, is moved to another camp for their entire training period. During the 5th week of training, recruits are assigned to working details (service week) throughout the entire recruit training complex including the processing area.

The housing in the processing area consists of wooden open-bay barracks. All recruits eat at the same galley. New recruits being processed intermingle with recruits in the 5th week of training. In the training area they are housed in permanent, brick "H"-type barracks. Each barrack holds one battalion of 12 companies, and each company lives in a large open-bay dormitory separated from all other training companies. Each pair of "sister" companies share lounge facilities and attend classes together.

A modern permanent dispensary with facilities for outpatient and inpatient care is located within the recruit training area. Within this dispensary is a field laboratory of the NAMRU-4 Epidemiology Division. During recruit processing and training, immunizations and prophylactic treatments are given (Fig. 4). Sick call is held three times a day, and a recruit may seek treatment at any of these times. If treated as an outpatient, an individual permanent record is made of each visit noting such data as symptoms, findings, treatment, and disposition. Daily official records report those men admitted to the sick list for inpatient care, as well as their admission diagnoses. Such illness data on each recruit in training is abstracted and transcribed to machine punched cards. It must be recognized that data from a longitudinal surveillance program may be influenced by admission policies, assessment of illness by individual physicians, and the availability of beds.

Surveillance Population

The surveillance program to be described commenced in October, 1964 and is conducted on a company basis. These companies have approximately 80 men and begin recruit training shortly after arrival at Great Lakes. Companies designated for surveillance are selected randomly and do not differ from their cohort companies with respect to training, berthing, and messing facilities. In contrast to other companies in training, routine immunizations are delayed until the 5th week of training. Influenza vaccination and the prophylactic drugs, sulfadiazine and Bicillin are not given to these companies.

Surveillance subjects previously were excluded from any research programs. Continuous surveillance was achieved by selecting new companies just after the preceding company completed training. The time in which any one surveillance company is observed is shown in Figure 5. However, a need for more intensive surveillance was recognized in January, 1966, and additional companies were sampled to provide parallel studies, thus insuring more complete data.

In addition to the monthly company surveillance, approximately 9 men a week are selected at sick call to provide samples for viral and serologic surveillance (ESS study). The 9 men a week are selected from the following patients: 3 men with febrile respiratory disease; 3 men with ARD, but afebrile, and 3 men who are afebrile and have no respiratory-related complaints. Acute and convalescent (21-day) bloods are collected from each man along with viral sampling. Sera are stored at -20°C until tested. Viral isolation attempts are directed toward recovering all viruses thought to be associated with respiratory diseases.

Serologic Sampling and Methods for Antibody Determination

Blood samples are collected two days after company formation, at mid-training, and before graduation. Subjects are sampled when hospitalized to

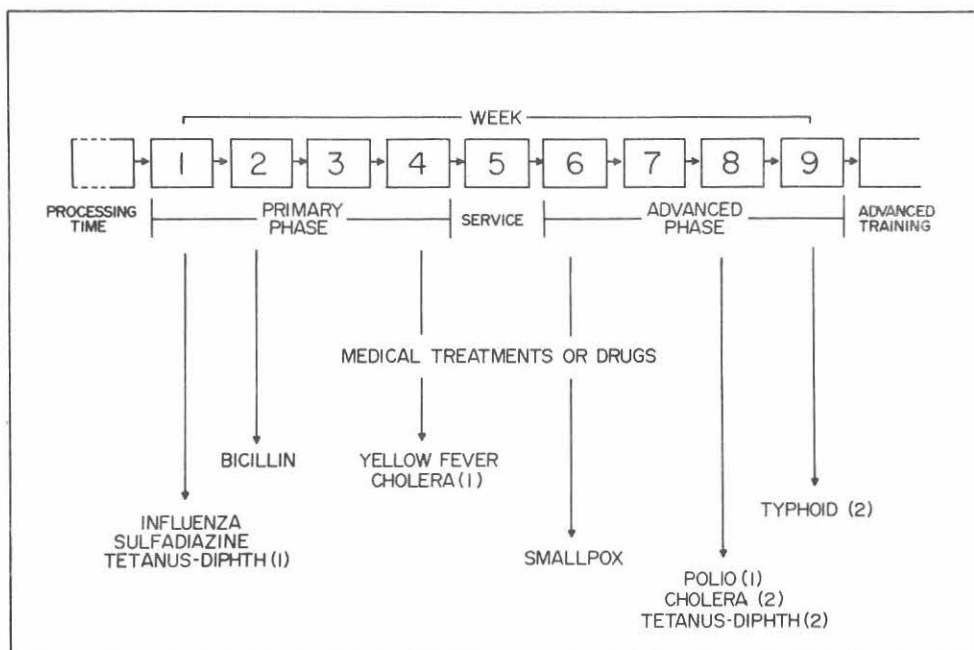


Fig. 4. Sequence of administration of immunizations and prophylactic drugs during the nine week training cycle, Great Lakes.

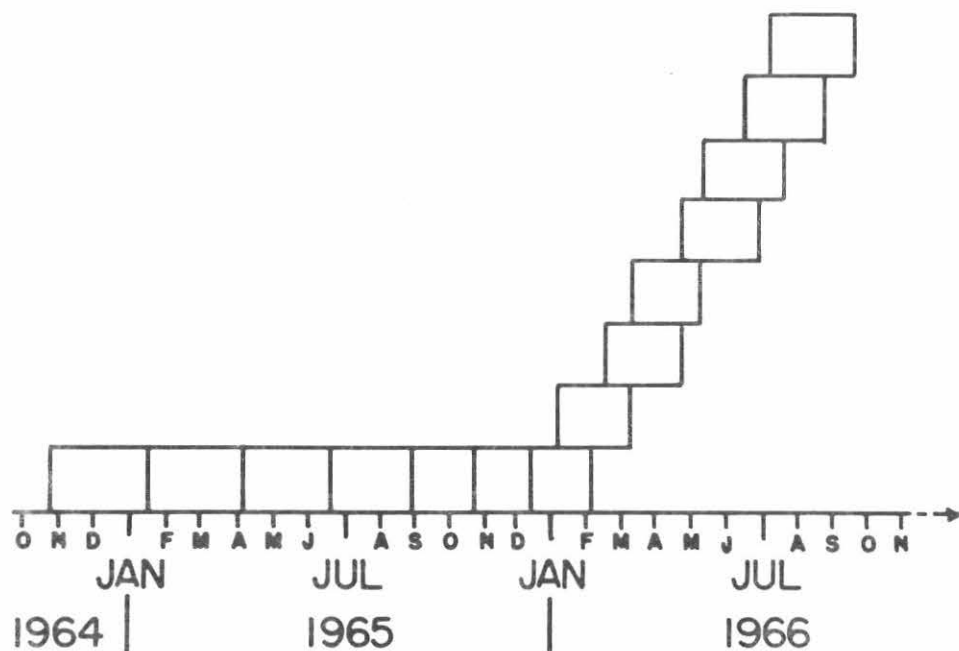


Fig. 5. The period in time represented by surveillance companies, Great Lakes, 1964 - 1966.

determine evidence of infection by isolation of the microbial agent or by determination of a 4-fold or greater seroconversion between acute and convalescent sera. Sera are separated from clotted blood shortly after sampling, aliquoted and stored at -20° C until tested. All serological tests are performed using standard procedures and the microtiter technique.

Mycoplasmal and Bacterial Sampling and Isolation

Sampling of Mycoplasma pneumoniae is done at the beginning of training, mid-training, and prior to graduation. If the recruit is admitted for hospital care, a sample is taken within 24 hours of admission and cultured. Colonies are examined at 10, 20 and 30 days for colonies of mycoplasma. If colonies are present at any of these times, they are tested for color change on PPL0 agar containing 0.2% 2,3,5-Triphenyl-2H-tetrazolium. Identification of the colonies is then confirmed by specific inhibition of growth in the presence of species-specific antisera.

Cultures for streptococci and meningococci are obtained at the same time as for M. pneumoniae. Beta-hemolytic streptococci are grouped and typed using precipitation methods. Meningococci are identified by slide agglutination tests using group-specific antisera.

Virus Isolation

Throat swab, rectal swab and a nasal washing specimen are obtained from each hospitalized recruit. This variety of specimens maximizes the types of viruses which can be isolated. All specimens are frozen and stored at -60° C upon arrival at the laboratory, and thawed immediately prior to use. HeLa (or HEp-2), diploid lung fibroblasts (WI-38) and primary monkey kidney tissue cultures are utilized routinely for virus recovery. Generally, the HeLa cells are most sensitive for adenoviruses, herpesvirus, respiratory syncytial and enteroviruses; WI-38 cells are optimal for rhinoviruses; and primary rhesus monkey kidney (MK) cells for myxoviruses. Should cytopathic effect (CPE) be noted, the culture is harvested and frozen for second passage. When CPE is not observed for two weeks, a blind second passage of similar duration is made. Cultures are tested for hemadsorption with guinea pig erythrocytes; those with extensive evidence of hemadsorption are frozen and stored for further passage.

When sufficient virus titers by CPE or hemadsorption are attained, the infecting agents are identified by neutralization or hemadsorption-inhibition tests with type-specific hyperimmune animal sera using the micro tissue culture method. When the characteristic CPE of rhinovirus in WI-38 appears, a presumptive diagnosis is made using the acid sensitivity test and then is classified as H or M strains by adaptability to growth on human or monkey cells, respectively. The final identification

is confirmed by neutralization tests.

Streptococcal Disease

Since institution of the Bicillin prophylaxis program, whereby all recruits receive 1.2 million units of Bicillin in the second week of training, streptococcal disease has ceased to be a problem. Streptococcal isolation rates have been less than three percent in surveillance companies which do not receive the Bicillin prophylaxis. Anti-streptolysin O (ASO) titer conversion rates have averaged, over the six years of surveillance program, from a high of eight percent to a low of 3.5 percent. However, within a single company, streptococcal ASO conversion rates have been as high as 20 percent (Fig. 6). Because of the low incidence of streptococcal infections and the small sample size, these data are not statistically significant, but do suggest that streptococcal infections may occur at any time of the year.

During this surveillance program, which has included tests on approximately 4800 recruits over a period of six years, only one recruit developed rheumatic fever. This recruit became ill during recruit leave and subsequently was admitted to the hospital. ASO serology revealed a significant increase in titer (58 to 192 Todd units) from serum collected at the beginning and end of recruit training and increased to 748 units upon admission to the hospital. A culture for streptococci was negative at graduation. There have been no cases of rheumatic fever in the recruit population receiving Bicillin since 1965. The sequelae of streptococcal infections in recruits have been virtually eliminated by the prophylactic program.

Viral Infections

Incidence of total adenovirus infection is measured serologically from specimens obtained in the company surveillance program. The highest incidence of adenovirus infection consistently occurred during the winter months with little evidence of infection during the summer and early fall period until 1968. Since 1968, a high incidence of adenovirus infection has occurred with the greatest frequency. It is believed that many of the responses to type 7 antigen were heterologous to the type 4 infection. The exception to this occurred soon after the live adenovirus vaccine was employed during 1966. The increase of adenovirus type 7 infections at that time is thought to have been due to a replacement of etiological types provoked by the use of adenovirus type 4 vaccine. This replacement effect has not been seen on two other occasions (1965, 1967) when live adenovirus type 4 vaccine was given to recruits.

The results of the two surveillance programs for viral isolation are shown in Figures 7-14. Virus isolations from surveillance company

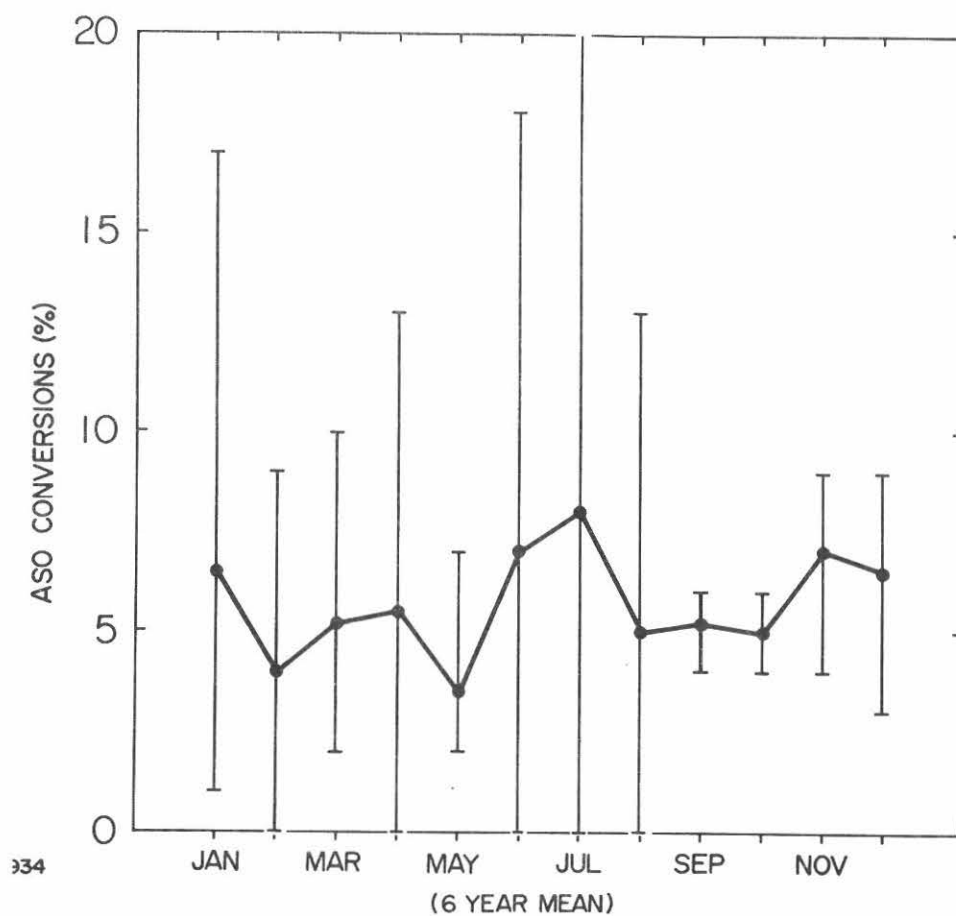


Fig. 6. Antistreptolysin O conversion rates in navy recruits by month of training, Great Lakes, 1965 - 1970.

recruits (CS) are presented in Figures 7 and 8. These data are derived from men who were admitted to the dispensary with symptoms of acute respiratory disease for the period 1964-1970. Shown in Figure 7 are the percent of samples positive for adenovirus and proportion of isolates identified as type 4 or 7. These data are four-month averages for each of the six years of surveillance. The digits within the bars are the number of samples collected and tested for each respective period. In general, the greatest number of admissions occurred in the winter months (November-February), declined in the spring (March-June) and were lowest in the summer and fall (July-October). Since 1968, there has been a considerable reduction in the number of men admitted. This is due more to a change in the admission policy rather than in actual reduction of ARD incidence.

These data show that adenovirus types 4 and 7 were associated with 65 percent of the ARD with a range of 0-100 percent. There was only one period (July-October 1967) in which these viruses were not isolated. Of the two adenoviruses, type 4 was isolated more often than type 7. Significantly, in only one year did the number of type 7 isolates predominate. This occurred during and after the institution of live adenovirus type 4 vaccine in February-June of 1966. When the prophylaxis program began in February, both type 4 and type 7 were being shed in equal numbers. Later, type 4 isolates decreased sharply and type 7 increased and predominated for the next eight months. It should be pointed out that none of these surveillance subjects received the type 4 vaccine from which heterologous protection might have been derived. Furthermore, ARD admission rates of the immunized recruits in the vaccine study declined abruptly after the program began and remained low during the next four months. Only in vaccine placebo subjects did the ARD rates approach numbers obtained from a previous nine-year average. During the 4 years following the 1966 vaccine program, the percentage of specimens positive for adenovirus returned to the high incidence previously seen and type 4 isolates were more frequent.

Figure 8 shows the numerical distribution of viruses other than adenovirus isolated from the CS survey. Of the various viral groups recovered, only the influenza viruses appear to have had any etiological significance. These samples were obtained from recruits with rather severe ARD requiring hospitalization. Agents associated with milder disease or common colds would not be expected to be isolated in large numbers.

Severe illnesses or increased hospital admissions, due to influenza disease, have not been seen in the recruit population since 1957. However, serological data indicate many subclinical influenza infections have occurred. The data shown in Figure 9 give a five-year mean incidence (1966-1970) of influenza A₂ or B infections. The highest seroconversion rates to influenza A₂ occurred during the months of November

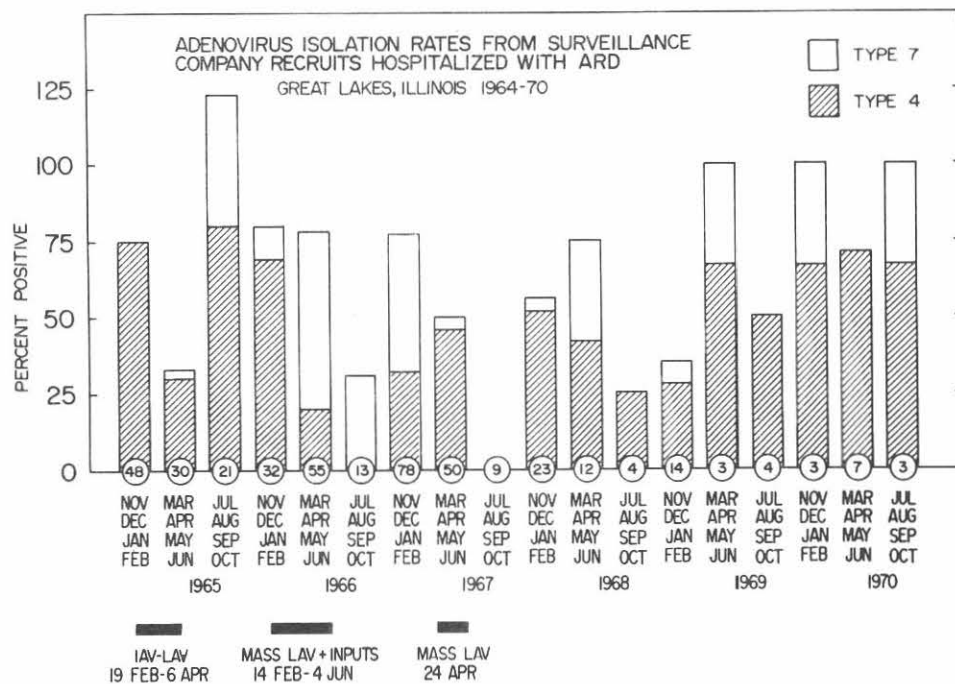


Fig. 7. Adenovirus types 4 and 7 isolation rates from surveillance company recruits hospitalized with ARD, Great Lakes, 1964-1970.

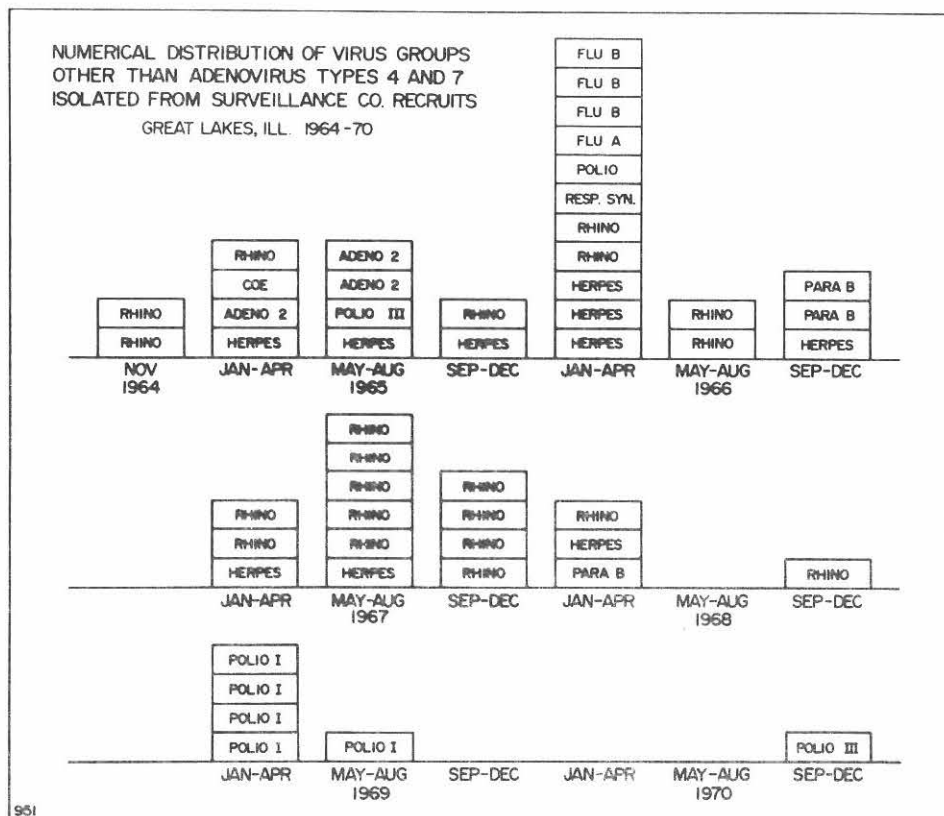


Fig. 8. Numerical distribution of virus groups other than adeno-virus types 4 and 7 isolated from surveillance company recruits, Great Lakes, 1964 - 1970.

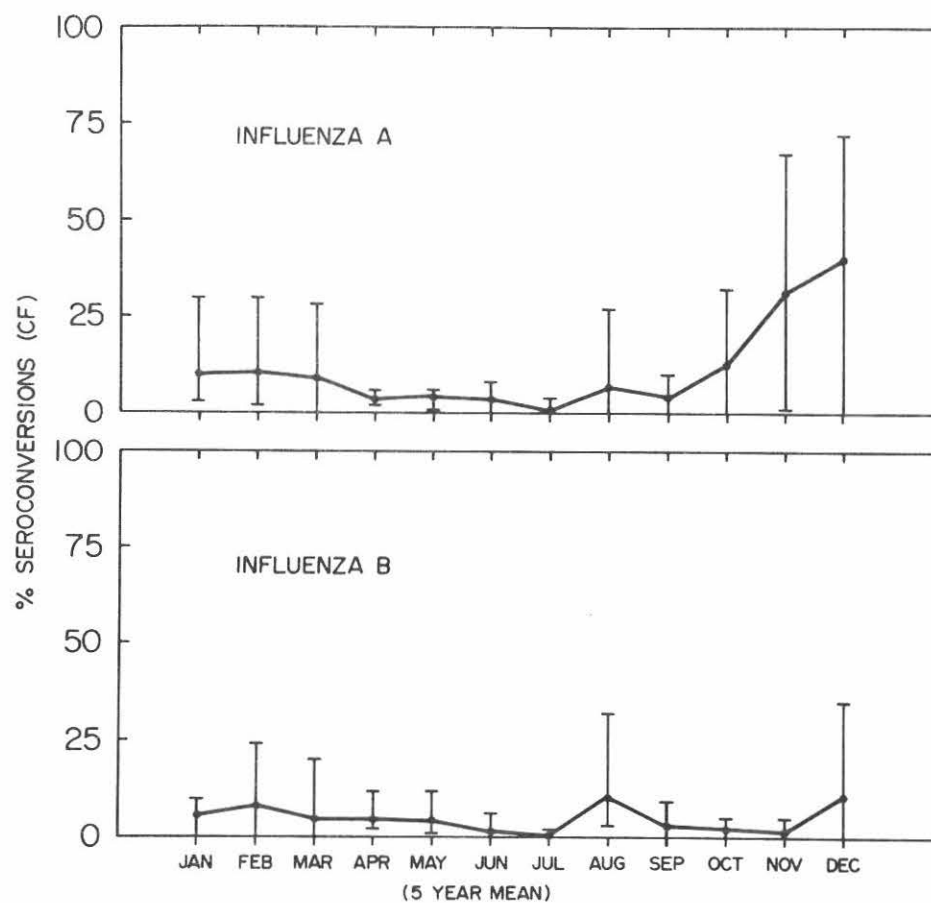


Fig. 9. Influenza A and B infections in navy recruits, Great Lakes, 1966 - 1970.

and December (31 and 40 percent, respectively). The seroconversion rates for A₂ in November and December of 1967-1969 were as high as 50 and 70 percent, while the same periods during 1965-1966 were essentially free of influenza infections. In two years, evidence of influenza infections occurred as early as August without developing into an epidemic. These outbreaks may have been aborted by the continuous influenza prophylaxis of incoming recruits. Seroconversion rates to influenza B during the early winter months of November and December have never reached the magnitude of influenza A₂. There was no increase in reported illnesses which could be related to the high seroconversion rates during the six years of surveillance.

The five-year means of serological conversion rates to rhinovirus infections in the surveillance population are presented in Figure 10. Only three antigens of the rhinovirus serogroups were employed in this study (1A, 1B and 2). Type 2 rhinovirus infections were the most prevalent in this population by serological surveillance. Peak infection rates were usually noted in the spring and fall months and have been observed to be as high as 60 percent. Rhinovirus types 1A and 1B have also been endemic in the study population, but to a lesser extent than type 2. The combined serological data indicate that these infections are common (25 percent incidence) in this population.

Figures 11-14 present background and virus isolation data obtained from recruits, not necessarily from survey companies, with respiratory or non-respiratory complaints, who reported to the dispensary (ESS study, 1966-1970). The data are based on an average of 160 samples for each of the four-month periods of the four-year study. Figure 11 shows the distribution of samples collected during 1968, according to the recruits' week of training. More individuals sought treatment for ARD in their third week of training than any other time, while recruits with non-respiratory complaints appeared for treatment about one week earlier.

Figure 12 shows the proportions of types 4 and 7 adenoviruses isolated from patients seen at sick call regardless of their clinical condition. About 36 percent of the samples were positive for adenoviruses, approximately half that observed in the CS survey. This is to be expected since the company surveillance data deals only with those recruits having ARD admissions. With the exception of the November and December period of 1966, adenovirus type 4 was the most common isolate, with the ratio of type 4 to type 7 approximately 3:1.

As previously shown in the CS studies (Fig. 7), the months with the highest total adenovirus isolation rates during the 1966-1970 period of observation were November and February and the lowest, July through October. After a second mass adenovirus vaccine administration on 24 April, 1967, specimens positive for adenovirus declined to the lowest

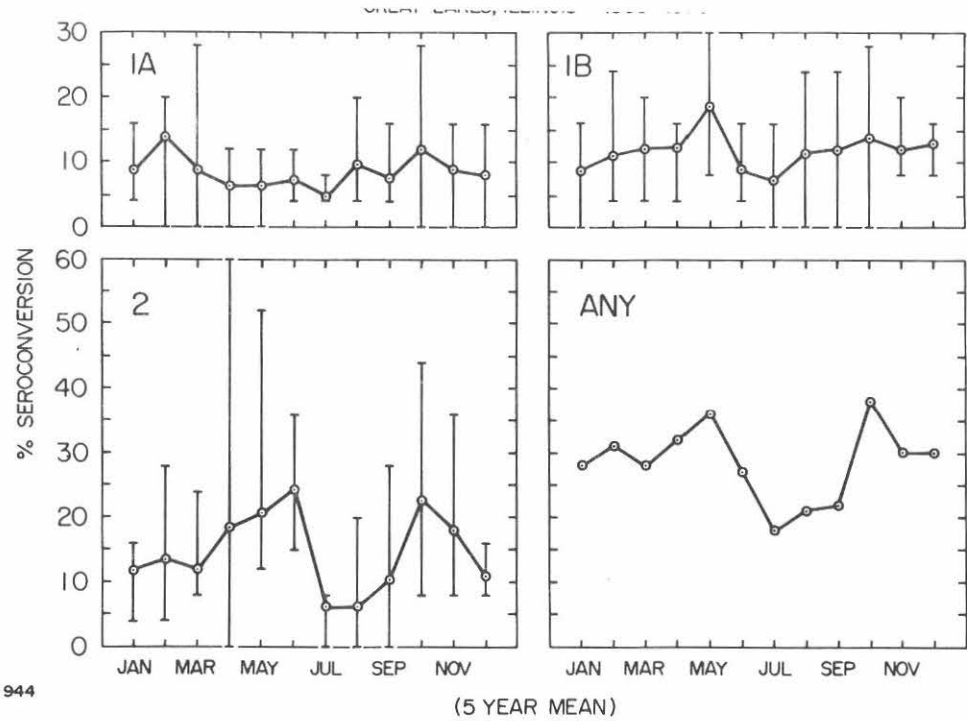


Fig. 10. Rhinovirus types 1A, 1B and 2 infections during recruit training, Great Lakes, 1966 - 1970.

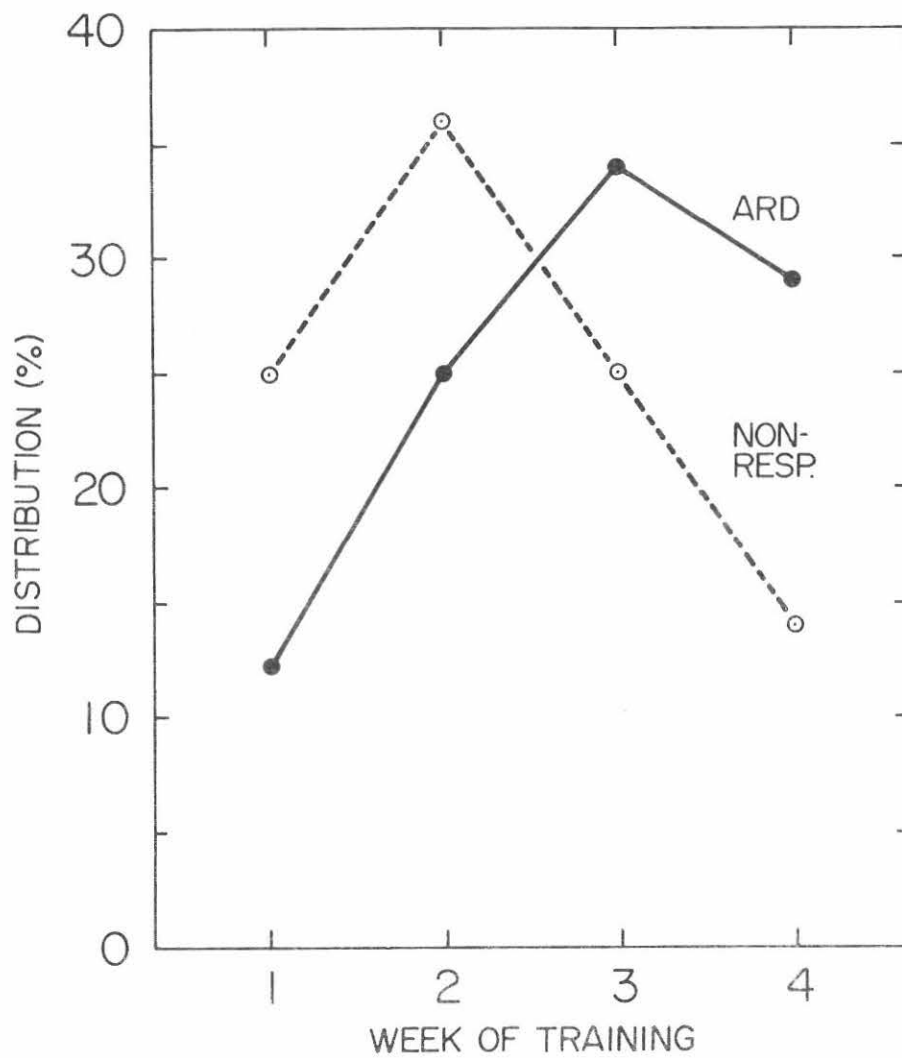


Fig. 11. Distribution of samples taken during Extra Surveillance Study (ESS) by week of training, Great Lakes, 1968.

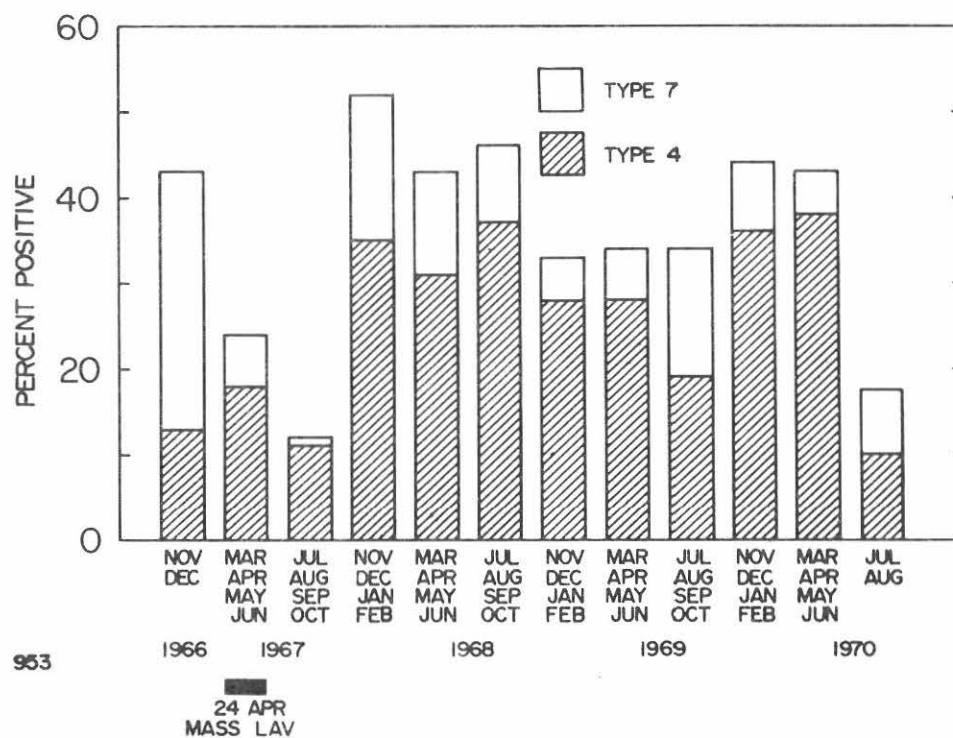


Fig. 12. Adenovirus types 4 and 7 isolation rates from patients sampled at sick call, ESS, Great Lakes, 1966 - 1970.

incidence ever observed in July to October, 1967.

Unlike the replacement effect noted after the first mass vaccination program in 1966, no ESS evidence was obtained either from laboratory or clinical data that type 7 had replaced type 4 (Fig. 12), nor did CS isolation data for this time period (April through October, 1967) show such an effect (Fig. 7). This may have been due to any of the following: 1) in 1967, live type 4 vaccine was administered just prior to the period when overall adenovirus infections tend to be low; 2) a lack of type 7 infections in the population when the vaccine was given; 3) since only recruits in the first four weeks of training were vaccinated and no attempt was made to continue prophylaxis for incoming recruits, there was insufficient "immunological pressure" to produce a replacement effect.

Figure 13 compares the distribution of adenoviruses isolated from men with either respiratory or non-respiratory complaints. The ratio of adenovirus isolations between the two clinical categories is approximately 3:1 in favor of samples from recruits with respiratory disease. Forty-four percent of these samples yielded adenovirus compared to 16 percent in specimens from men with non-respiratory complaints. As shown in Figure 12, adenovirus type 4 was identified in 70 to 75 percent of the positive specimens from patients in either clinical category. The exceptions to this type 4 predominance were in those samples collected in November and December of 1966, after the live adenovirus program which ended in June of that year. More type 7 (Fig. 13) was isolated again from non-respiratory patients after live adenovirus type 4 vaccine was administered in a single day (24 April, 1967).

Figure 14 shows the distribution of adenovirus when recruits with respiratory disease are further subdivided into febrile and afebrile categories. Almost 70 percent of the samples from febrile ARD patients yielded adenoviruses. This does compare favorably to the 64 percent positive yield obtained in the CS survey. Those specimens from the afebrile ARD category were less positive for adenovirus, but more so than the samples from non-respiratory patients. The distribution of adenovirus types 4 and 7 is similar to that shown in Figure 7.

Table I shows the distribution of groups and numbers of viruses other than adenovirus types 4 and 7 which were recovered during the four-year ESS study. Rhinoviruses were more frequently isolated than any other group with the exception of the polioviruses, which probably occurred secondary to administration of live oral poliovirus vaccine. The incidences of other agents were too low to imply any significant etiological role. Surprisingly, myxoviruses, particularly influenza, were found in only a few instances despite the large number of serological conversions observed.

Rubella

Before the nationwide rubella epidemic of 1964, this disease was the

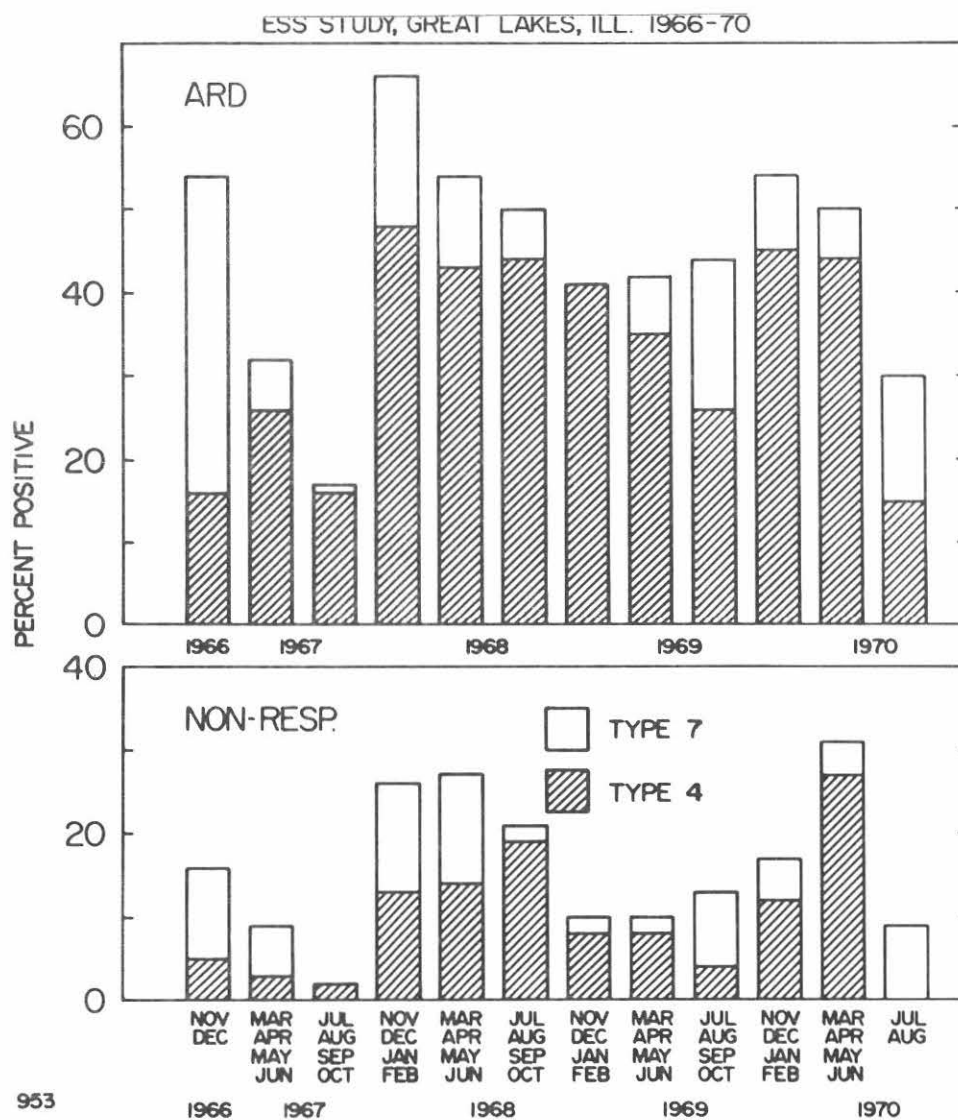


Fig. 13. Distribution of adenovirus types 4 and 7 isolations from recruits with ARD and with non-respiratory complaints, ESS, Great Lakes, 1966 - 1970.

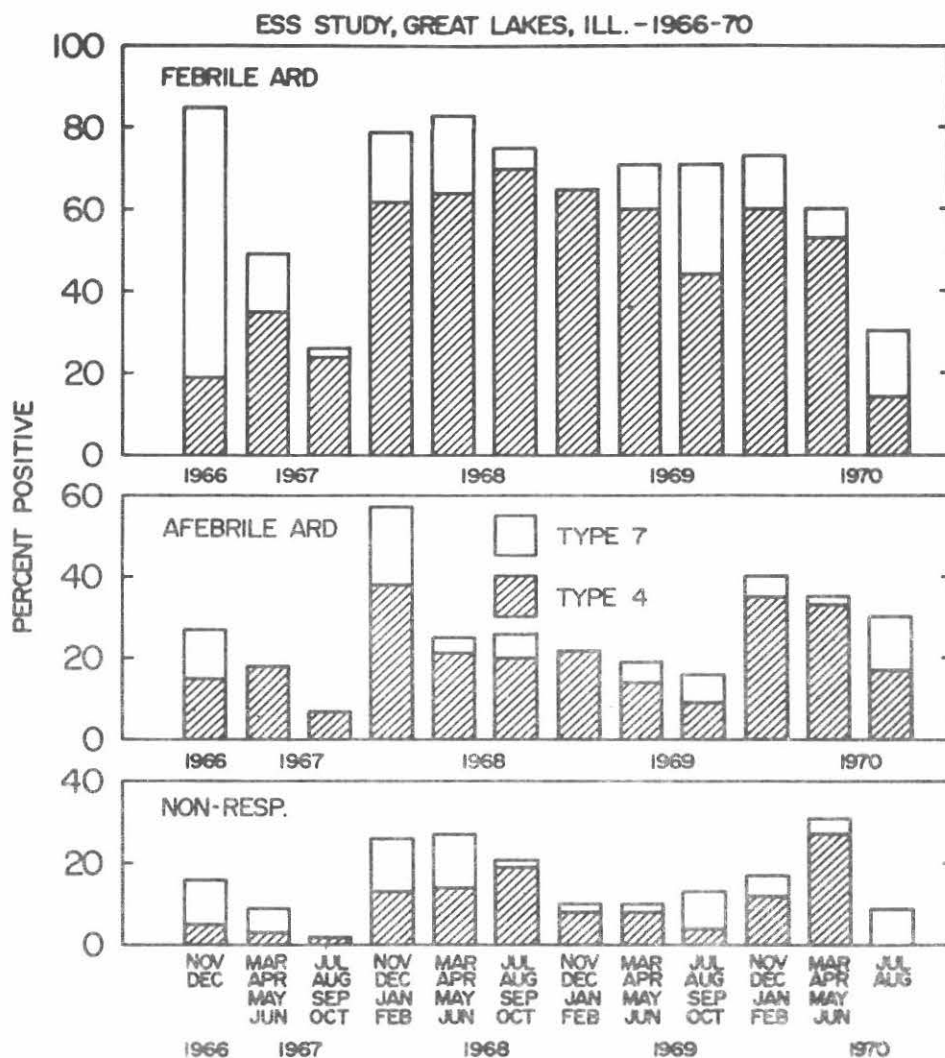


Fig. 14. Distribution of adenovirus types 4 and 7 isolations from recruits with febrile ARD, afebrile ARD, and non-respiratory complaints, ESS, Great Lakes, 1966 - 1970.

Table I. Numerical Distribution of Virus Groups Other Than Adenovirus Types 4 and 7 Isolated From Sick Call Samples (Extra Surveillance Study, Great Lakes, 1966-1970)

	Rhinovirus	Adenovirus 2	Adenovirus 5	Herpesvirus	Poliovirus I	Poliovirus II	Poliovirus III	Unident. Polio	Para Flu 1	Para Flu 2	Para Flu 3	Coe	Flu A ₂ HK	Flu B Mass
Nov 1966	33	-	-	5	-	-	-	-	-	-	-	-	-	-
Jan-Apr 1967	40	-	-	4	-	-	-	-	-	-	-	-	-	-
Jan-Apr 1968	24	7	-	2	1	-	-	-	-	1	6	-	-	-
Jan-Apr 1969	12	-	-	-	-	25	1	12	-	-	-	1	-	-
Jan-Apr 1970	14	-	-	-	-	-	-	-	-	-	1	-	2	-
May-Aug 1967	59	1	2	-	4	4	5	-	1	-	-	-	-	-
May-Aug 1968	14	2	-	3	11	4	10	-	-	-	3	-	-	2
May-Aug 1969	11	1	-	1	22	7	8	-	-	-	4	-	-	-
May-Aug 1970	15	1	-	2	2	1	2	15	-	-	-	-	-	-
Sep-Dec 1967	43	-	-	3	2	1	3	-	-	-	2	7	-	-
Sep-Dec 1968	15	1	-	1	31	8	8	-	1	-	1	-	3	-
Sep-Dec 1969	5	2	-	-	-	-	-	-	-	-	1	-	-	-
Sep 1970	2	-	-	-	-	-	1	-	-	-	-	-	-	-

second most frequent cause of hospitalization of recruits at Great Lakes. Three to five percent of recruits were admitted with rubella. Half of these cases occurred before the 4th week of training. Since 1964, rubella has ceased to be a major cause of recruit hospital admissions.

Limited information was available on the ratio of admissions to rubella infections in this population until the hemagglutination-inhibition (HI) test was developed. Using this test, a study was made of initial rubella antibody titers of recruits reporting for training during 1968-1970 and the seroconversion rate of these individuals after the 8-11 week training period. Such information should allow us to determine any changes in the susceptibility status of 17 to 20-year-olds, the extent of rubella infections in the recruit population, and the relationship between the number of infections and admitted clinical disease.

The number of men reporting for recruit training with an initial titer of less than 1:10 to 1:160 or greater is shown in Table II and Figure 15. There has been no appreciable shift in the distribution pattern of initial antibody titer levels over the three-year period. This consistent distribution shows that nine percent of the 17 to 20-year-old males have no detectable rubella HI antibody titer, suggesting that 91 percent of the recruit population is "immune" to rubella.

The percent of men showing a seroconversion to rubella is shown in Table III. From 63 to 81 percent of the men reporting with a titer of <1:10 show a seroconversion during recruit training. The three-year mean seroconversion rate for those recruits reporting with an initial titer of <1:10 is 73.4 percent (Table IV). Men reporting with titers of 1:10, 1:20, and 1:40 seroconverted at the following annual rates: 25.5, 10.5 and 3.3 percent, respectively. There were no seroconversions in those recruits who reported with a titer of 1:80 or greater.

The infection profile during the calendar year by initial rubella HI titer is shown in Figure 16. From November through June of each year, 50 to 92 percent of the susceptibles (initial titer <1:10) become infected. The infection rate during the summer-late summer period ranged from 50 to 60 percent. No attempt to associate survey seroconversion rates with clinical evidence of rubella infections has been made. The data suggest that a small percent of recruits with titers of 1:10 or greater became infected with rubella causing an increase in HI titer, especially in the winter-late winter period.

The data in Figure 16 point out that the seasonal pattern of rubella infections is like that of ARD. This suggests that there may be an association between the two illnesses promoted by mutual dissemination of respiratory tract viruses. Recruit training consists of an

Table II. Initial Rubella HI Titers in Men Reporting for Recruit Training, Great Lakes, 1968-1970

	1968			1969		1970	
	<u>Initial</u> <u>< Titer</u>	<u>Number</u>	<u>Percent</u> <u>Tested</u>	<u>Number</u>	<u>Percent</u> <u>Tested</u>	<u>Number</u>	<u>Percent</u> <u>Tested</u>
	1:10	52	9.2	52	9.0	52	8.8
	1:10	30	5.3	15	2.6	16	2.7
	1:20	87	15.4	56	9.7	47	8.0
	1:40	171	30.3	149	25.7	160	27.2
	1:80	140	24.8	154	26.6	185	31.5
	≥1:160	84	14.9	153	26.4	128	21.8
Total		564		579		588	

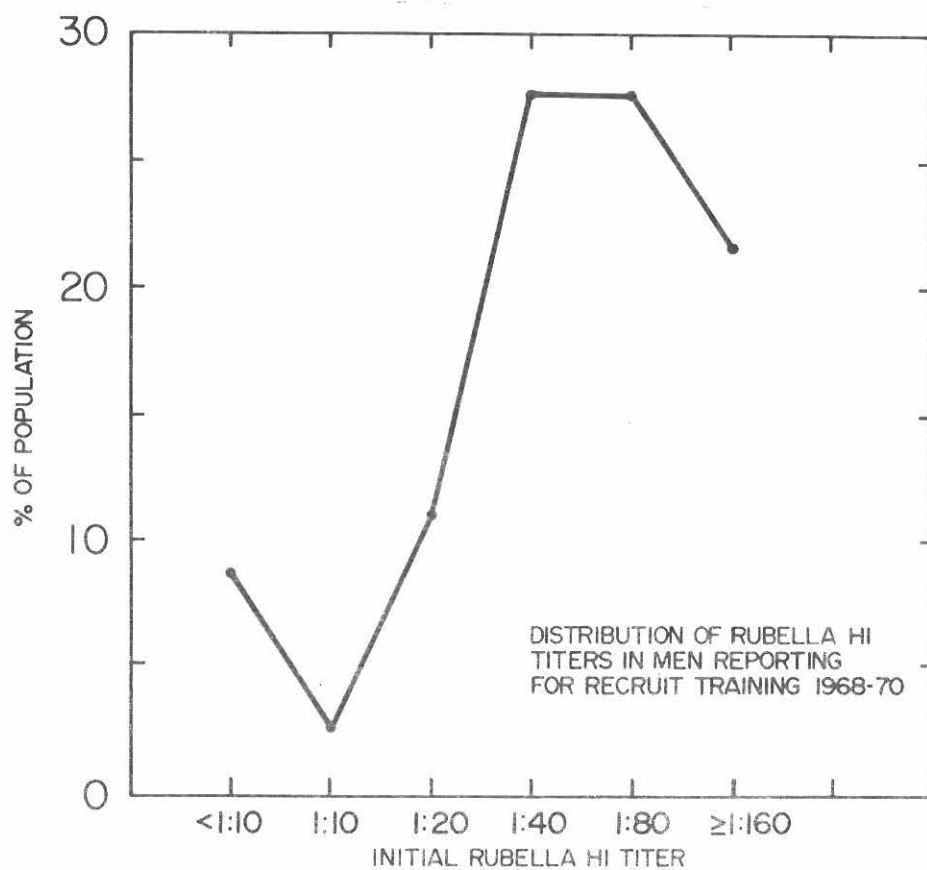


Fig. 15. Distribution of rubella HI titers in men reporting for recruit training, Great Lakes, 1968 - 1970.

Table III. Rubella HI Seroconversion Rate in Navy Recruits
According to Initial HI Titer and Year in Training,
Great Lakes, 1968-1970

<u>Initial titer</u>	<u>1968</u>	<u>1969</u>	<u>1970</u>
< 1:10	63.5	80.8	75.0
1:10	20.0	0	43.7
1:20	13.8	7.1	8.5
1:40	2.3	4.7	3.1
1:80	0	0	0
≥1:160	0	0	0
Mean sero- conversion rate	9.8	9.2	9.4

Table IV. Rubella Infections Experienced by Navy Recruits in
Training, Great Lakes, 1968-1970

<u>Initial titer</u>	<u>Number of men</u>	<u>% of men with titer</u>	<u>Rises 4-fold or greater</u>	<u>% of men with 4-fold rise</u>
< 1:10	154	9.0	113	73.4
1:10	47	2.7	12	25.5
1:20	190	11.1	20	10.5
1:40	480	27.9	16	3.3
1:80	479	27.9	0	0
≥1:160	368	21.4	0	0
Total	1718		161	
Overall seroconversion rate: $161/1718 = 9.4\%$				

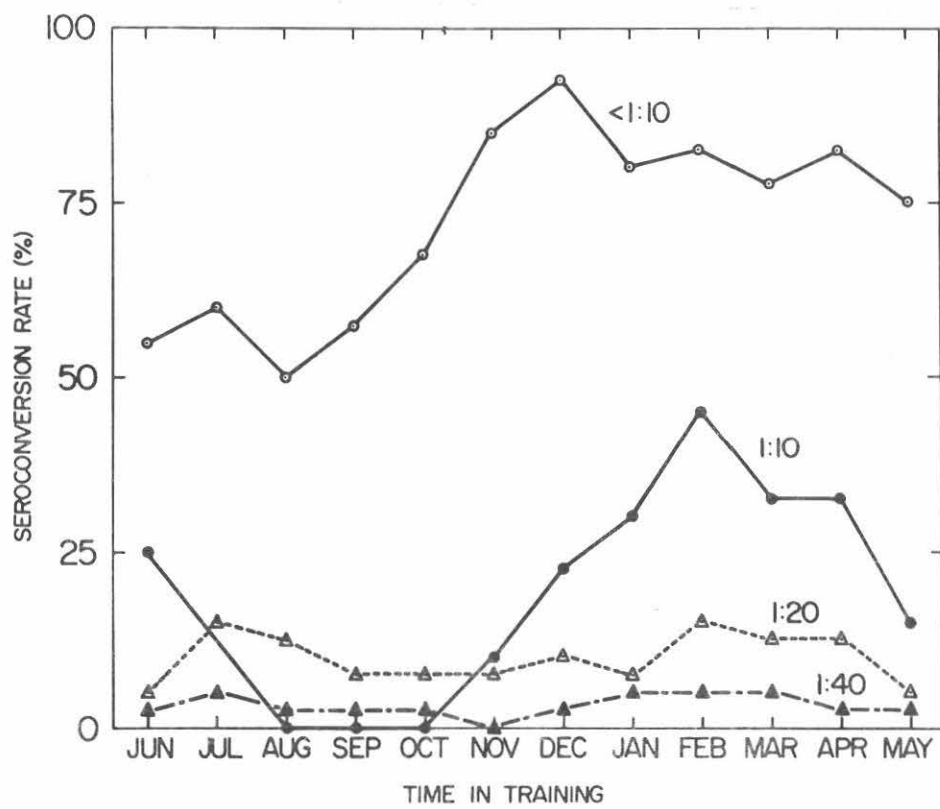


Fig. 16. Seroconversions by recruits to rubella infections by initial HI titer, Great Lakes, 1968 - 1970.

unusual environment where over 70 percent of susceptibles become infected in population where there are 90 percent immunes to rubella. This attests to the efficiency of dissemination of rubella virus in this population. To insure a "herd" effect immune population to rubella infection in recruits, probably close to 100 percent of the men would have to be immunized.

The "herd" immune effect observed in other populations is probably inoperative in the unusual environmental and epidemiological situation existing at recruit training centers. This also emphasizes the relationships between disease problems in military populations. Prevention of ARD could conceivably reduce the risk of other infection, such as rubella.

Mycoplasma Pneumoniae

The isolation of M. pneumoniae from patients admitted to the recruit dispensary pneumonia ward is shown in Figure 17. M. pneumoniae isolation rates ranged from a low of zero in the winter-spring season to a high of 30 percent during the late summer-early fall of 1969. This pattern of late summer-early fall increase in M. pneumoniae isolations has been consistent over the past five years.

The relationship between M. pneumoniae isolations from pneumonia and their seroconversion rates is shown in the bottom portion of Figure 18. In this year-long surveillance, sera was collected from the recruit upon admission to the pneumonia ward and a convalescent sample taken from one to three weeks post-admission. There is a good correlation between M. pneumoniae isolation and seroconversion in hospitalized patients. The data illustrated in the top portion of this figure emphasizes a lack of correlation between the incidence of pneumonia admissions and M. pneumoniae isolations during the year of June 1968 through August 1969.

The correlation between M. pneumoniae infections in the recruit population, as determined by the CF test and M. pneumoniae isolations from the same population, is shown in Figure 19. While the isolation rate is less than the seroconversion rate, the seasonal pattern is the same. These data indicate that M. pneumoniae is a late summer-early fall infection in the Great Lakes recruit population.

The same seasonal pattern, both in the seroconversion rate of the surveillance population and in M. pneumoniae isolations from recruits who were admitted with pneumonia, is shown in Figure 20. The data in Figures 19 and 20 also point out the low pathogenicity of a M. pneumoniae infection. It was estimated from the seroconversion rate to M. pneumoniae approximately 3,000 M. pneumoniae infections should have occurred during

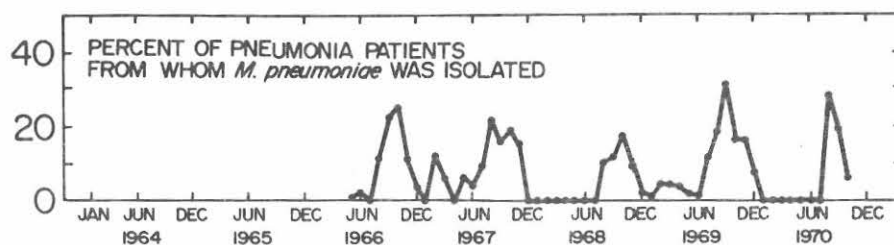


Fig. 17. Percent of pneumonia patients from whom *M. pneumoniae* was isolated, Great Lakes, 1964 - 1970.

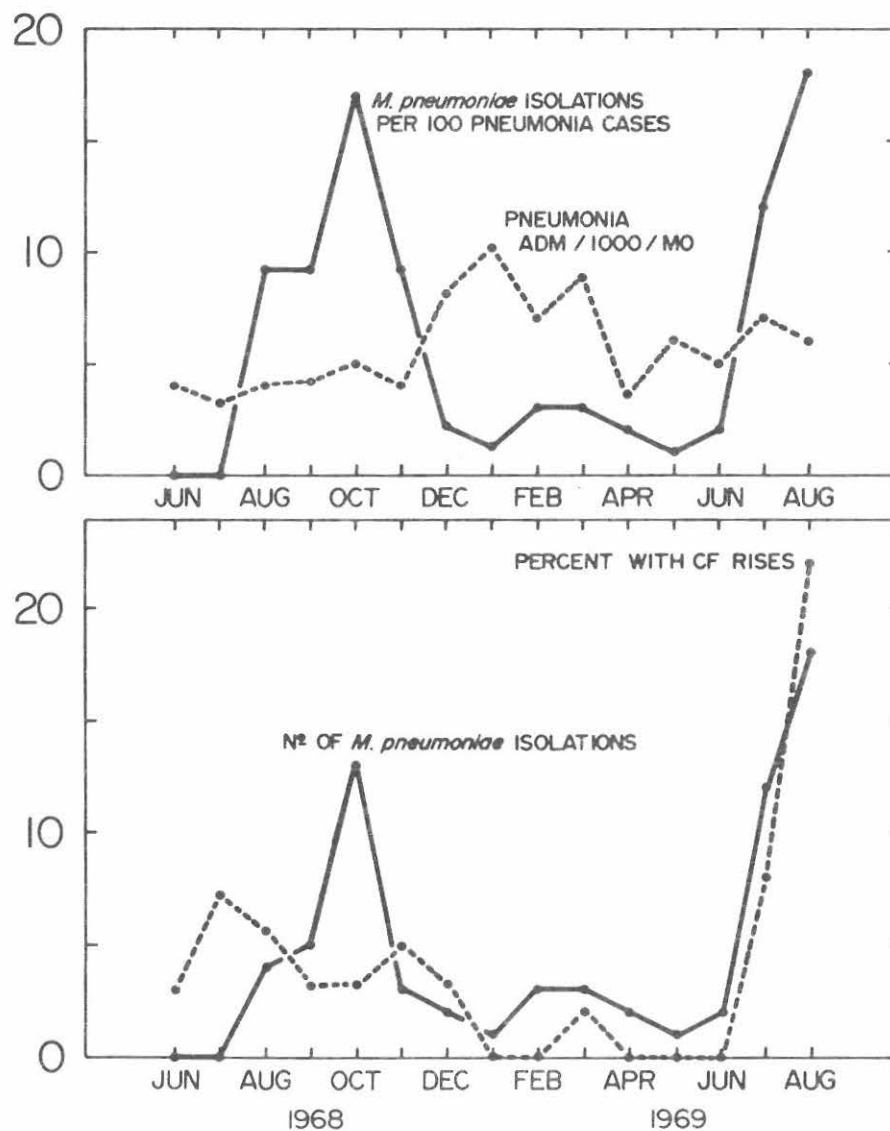


Fig. 18. Relationship of *M. pneumoniae* isolations, CF titer rises, and the pneumonia admission rate, Great Lakes, 1968-1969.

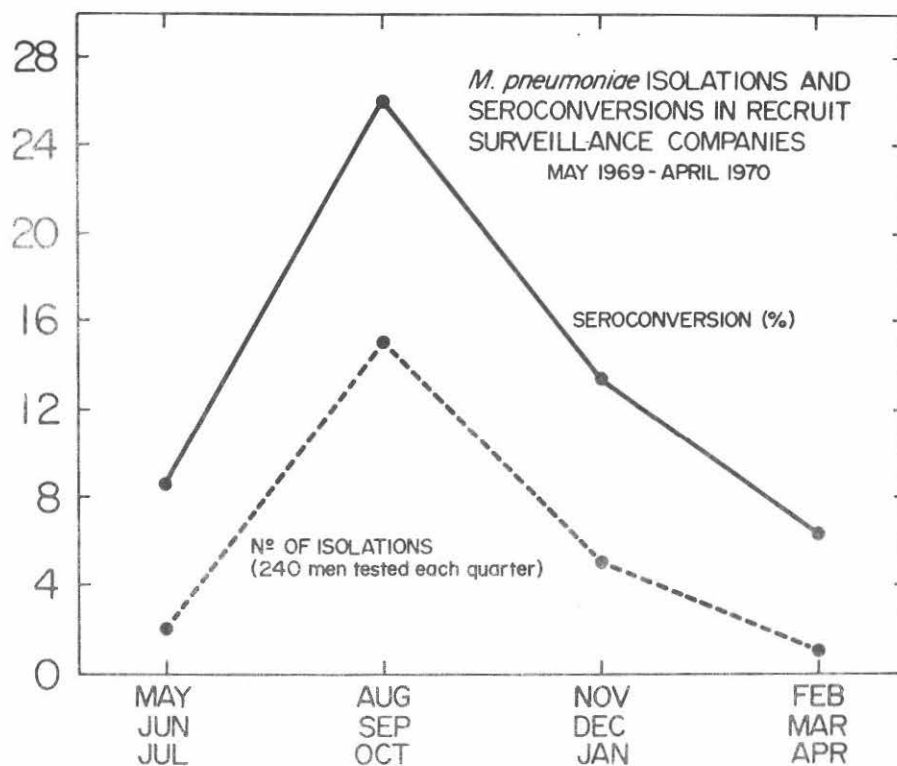


Fig. 19. Relationship of *M. pneumoniae* isolations to seroconversions in recruit surveillance companies, Great Lakes, by selected quarters of the year.

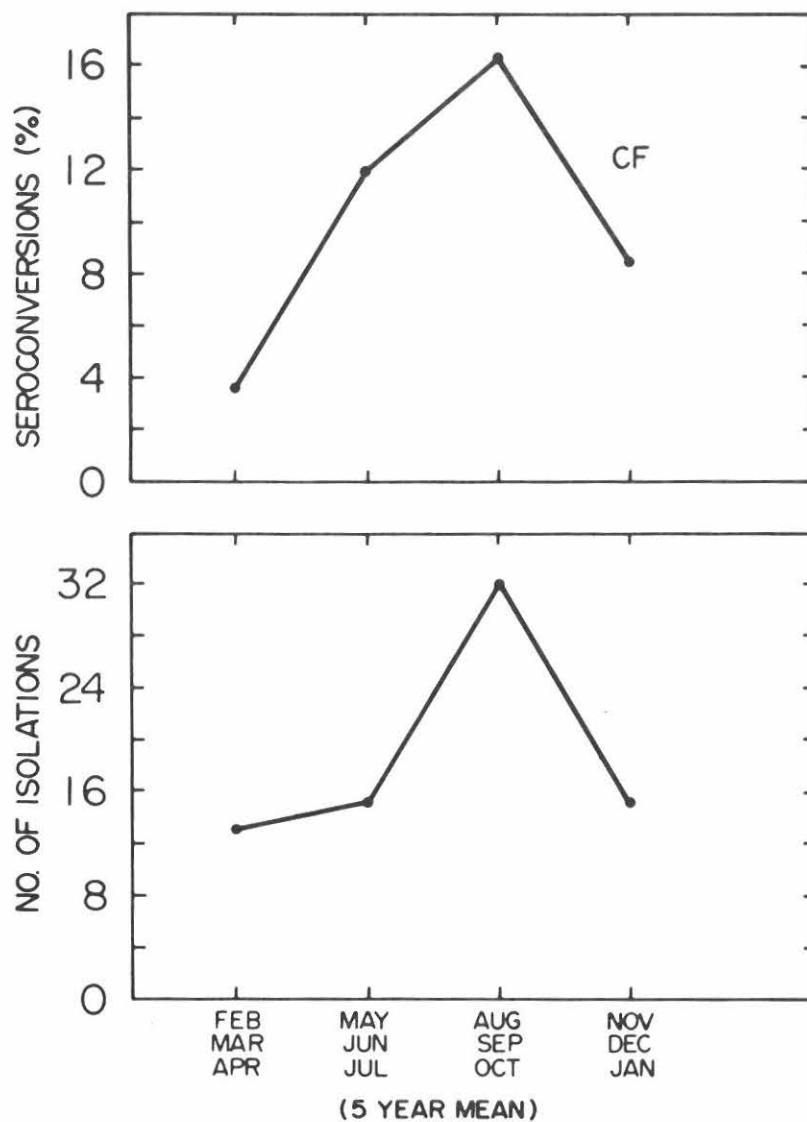


Fig. 20. Seasonal pattern of M. pneumoniae seroconversion and isolation in navy recruits, Great Lakes, by selected quarters of the year.

the months of August, September, and October during 1965 through 1970. Using the six-year mean pneumonia admission rate during August, September and October, about 900 pneumonia cases of all etiologies were admitted. Twenty percent of the pneumonia admissions showed a seroconversion to M. pneumoniae. Approximately one of 15 infected with M. pneumoniae was hospitalized with pneumonia.

The pattern of pneumonia admissions by week of training and seasons is shown in Figure 21. While the admission patterns for all seasons are similar, the admission profile during the late summer months (Sep, Oct, Nov) shows a slight extension beyond the 5th week of training. The isolation rate of M. pneumoniae from recruits admitted with pneumonia is also depicted. It is evident that mycoplasma pneumonias occur more frequently after the 4th week of training. That M. pneumoniae infection is not likely an extension of ARD is illustrated by the data in Figure 22. When the ARD rate is at its peak, M. pneumoniae seroconversions rates are at their lowest levels, suggesting the absence of that infectious agent in the population. Conversely, when seroconversion rates to M. pneumoniae are at a peak in the late summer-early fall, ARD rates are at their lowest levels of the year.

Meningococcal Surveillance

Meningococcal infections in the recruit population as determined by either the CF or the HA test are shown in Figure 23. A 4-fold or greater increase in titer was considered evidence of infection. The seroconversion rate varied from a low of five percent to a high of 90 percent during the period of this surveillance. There was a marked seasonal pattern in conversion rates from 1964 through 1967. Starting in 1968, this seasonal pattern has been modified in that the lower rates in summer have ranged from 25 to 40 percent rather than the five to ten percent experienced in the summers of 1966 and 1967. Serological evidence of group C infections did not occur until December 1967. The appearance of group C seroconversion coincided with the appearance of meningococcal disease due to group C. While most of the meningococcal disease since 1968 has been caused by group C, disease incidence has not shown a close relationship with group C seroconversion rates. As shown in Figure 23, during the year 1970, group C rates never exceeded 25 percent in any month, yet meningococcal disease incidence was higher during this time.

The seroconversion rates to group Y meningococcal infection are shown in the bottom segment of Figure 23. The rate of group Y meningococcus has been as high as 80 percent and group Y has been the predominant serological group isolated in the recruit population at Great Lakes. Since 1967, the sharp seasonal incidence of group Y infection has been modified to the extent that the rate in summer never has been

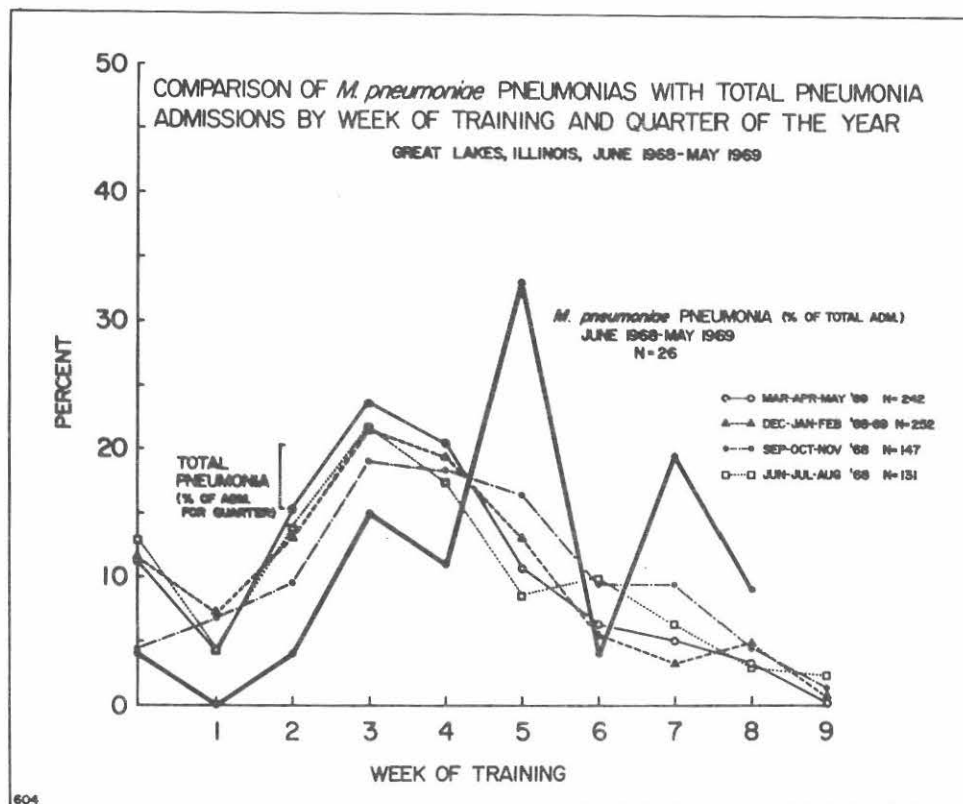


Fig. 21. Comparison of *M. pneumoniae* pneumonias with total pneumonia admissions, by week of training and by quarter of the year, Great Lakes, June 1968 - May 1969.

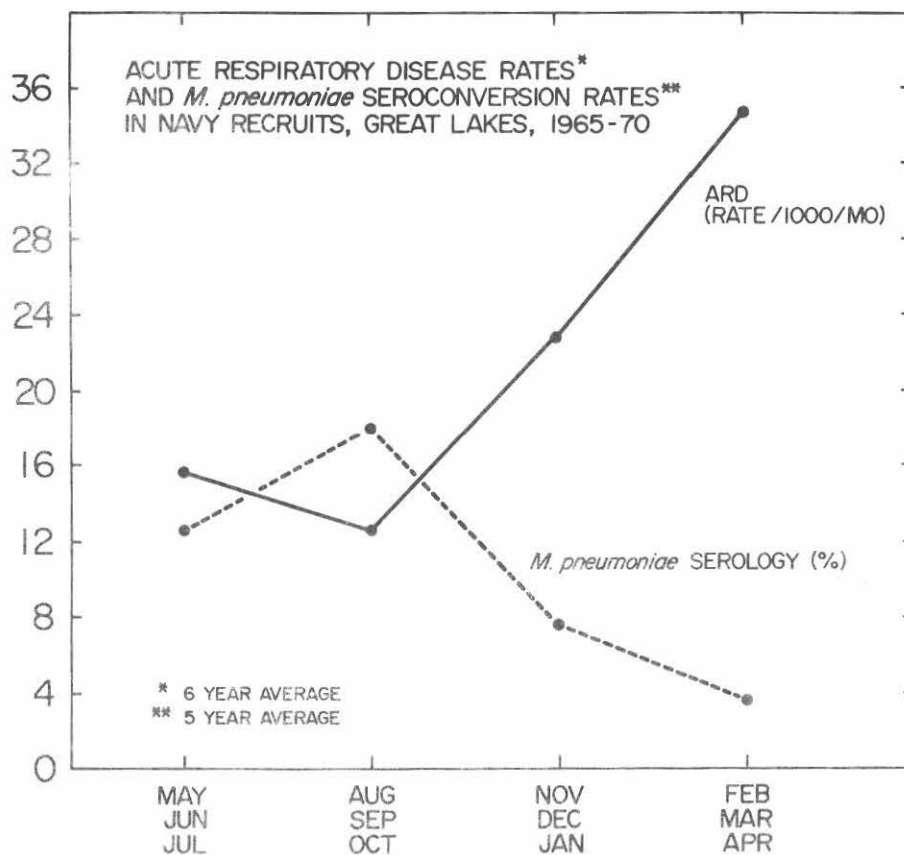


Fig. 22. ARD rates (6 yr average) and *M. pneumoniae* seroconversion rates (5 yr average) in navy recruits, Great Lakes, 1965 - 1970.

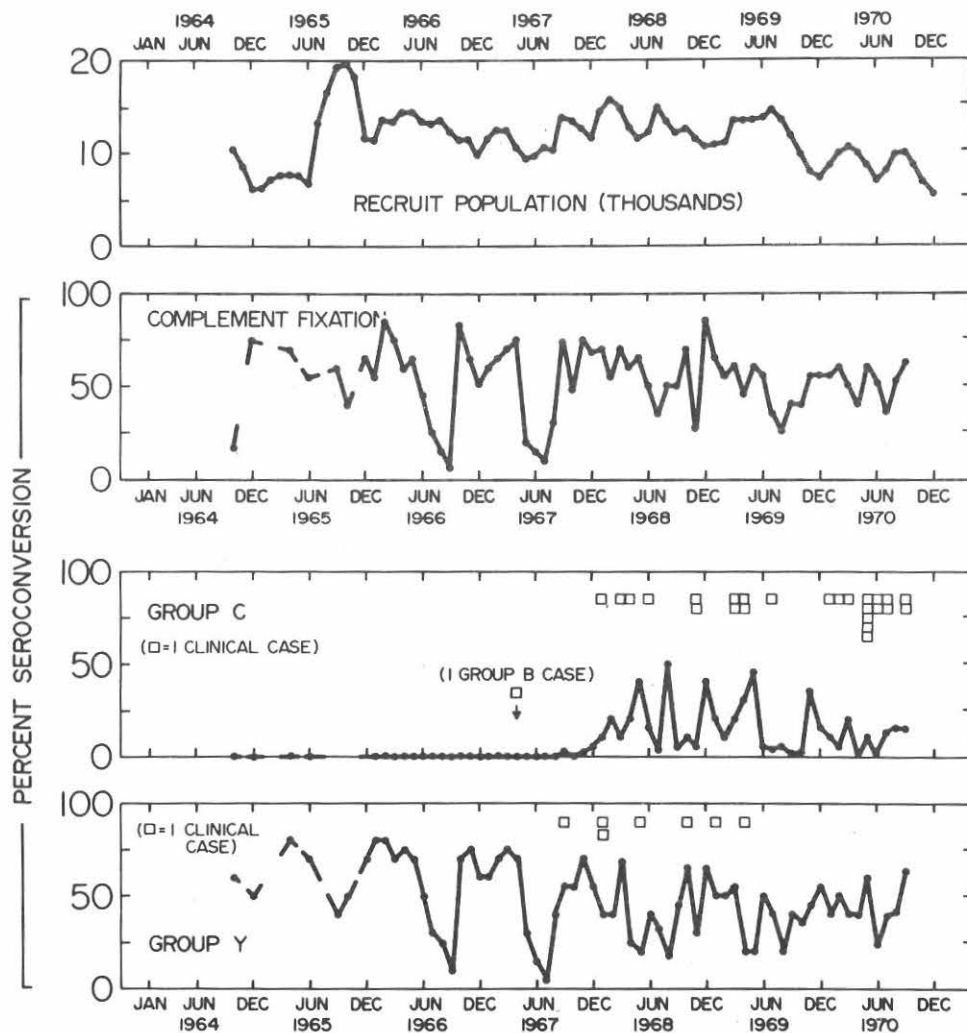


Fig. 23. Recruit population statistics, and seroconversion rates among recruits, 1964 - 1970. Clinical cases of meningococcal disease are indicated by squares.

lower than 25 percent. Only 7 cases of meningococcal disease, due to group Y, have occurred since 1967, although, from the serological data, approximately 50 percent of the men have become infected with group Y meningococci and probably were carriers. The disease/infection ratio is approximately 1:18,000.

The meningococcal serogroups isolated from all naval personnel at Great Lakes from June through May 1970 are shown in Table V. Data in this table include meningococcal isolations from incoming recruits, graduating recruits and men reporting to the Service School Command for advanced training. The predominant serological group isolated from naval personnel was group Y. The data show clearly that other serological groups were present and could have contributed to the incidence of meningococcal disease.

The percent of certain serogroups of meningococci isolated from naval personnel is shown in Table VI. Groups B and Y were isolated most frequently from men reporting for recruit training. Men arriving for advanced training at the Service School Command from other naval activities have shown an increased incidence of groups Y and C since June, 1969.

The percent of naval personnel who were or became carriers of meningococcal organisms are shown in Figure 24 and Table VII. Twenty-two percent of the men who entered recruit training were carrying some meningococcal serogroup in their nasopharynx. This monthly carrier rate pattern has been consistent since 1967. The seasonal pattern of meningococcal carrier rates is shown in Figure 24, and in Figure 25 where it is divided into groups Y and C. These data suggest that meningococci spread readily throughout the recruit population in all seasons except for a very short period of time during the late summer.

Sulfa-sensitivity tests conducted on all meningococcal strains isolated from men reporting for recruit training are shown in Table VIII and Figure 26. Group B strains became progressively less sulfa-resistant from 1967 through the first 6 months of 1970 (12.5 percent to 4.1 percent), but during the last 6 months of 1970 appeared to have become more resistant once again. A marked change in sulfadiazine-resistant group C strains is apparent with an increase from 22.2 percent to a high of 64.5 percent. This increase in sulfa resistance coincided with the appearance of group C meningococcal disease in the recruit population in January, 1968 (Fig. 23). The outbreak of sulfa-resistant group B meningococcal disease at NTC, San Diego in 1963 and the sulfa-resistant group C cases in military populations in later years strongly suggest that virulence may be positively correlated with sulfadiazine resistance.

A study was conducted on a recruit company entering training in January, 1968. Of the 76 recruits, 52 were negative for Neisseria

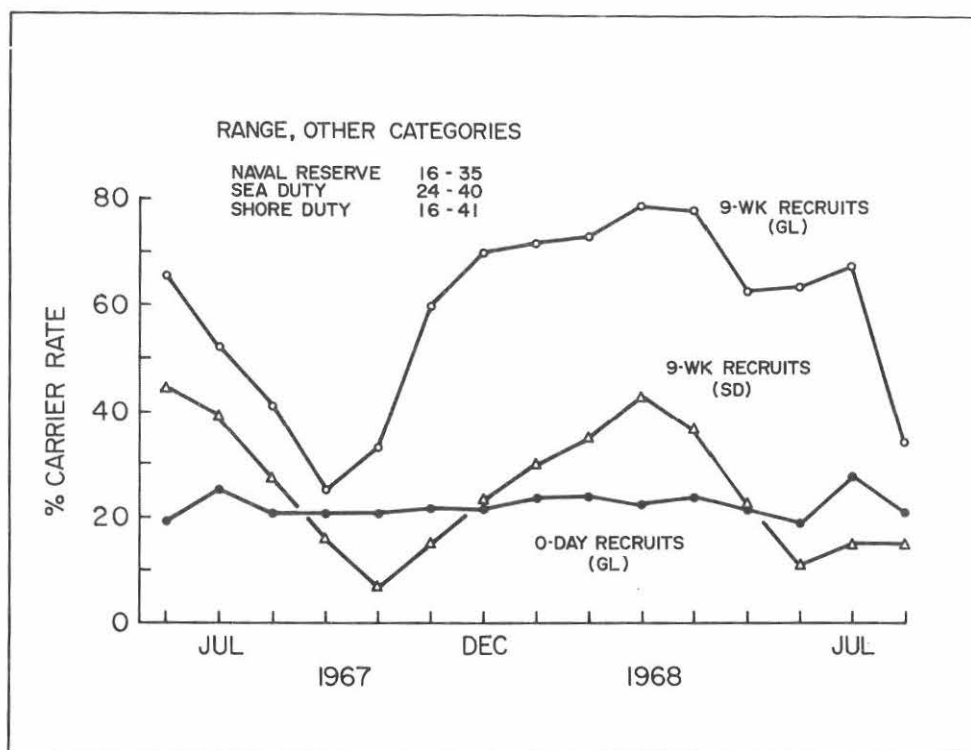


Fig. 24. Meningococcal carrier rates of navy recruits at the beginning and end of training at Great Lakes, and at the end of training at San Diego, 1967 - 1968.

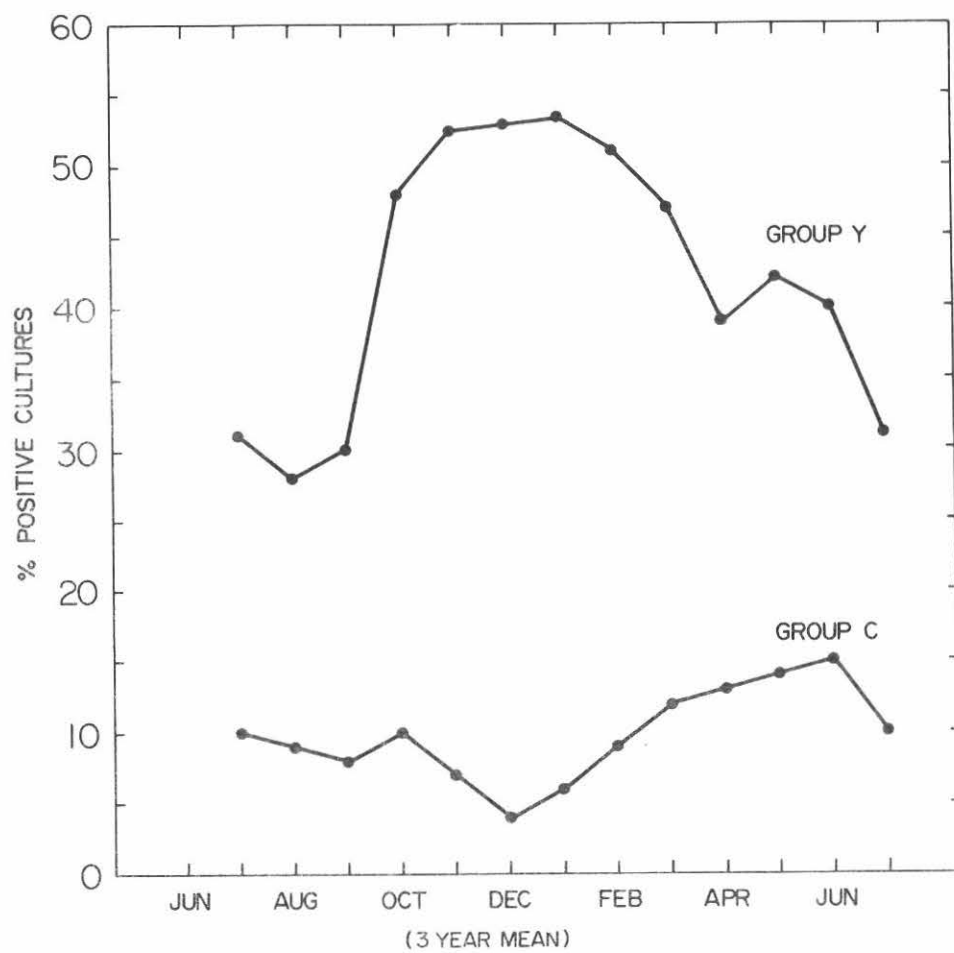


Fig. 25. Meningococcal carrier status of recruits graduating from recruit training, 1968 - 1970.

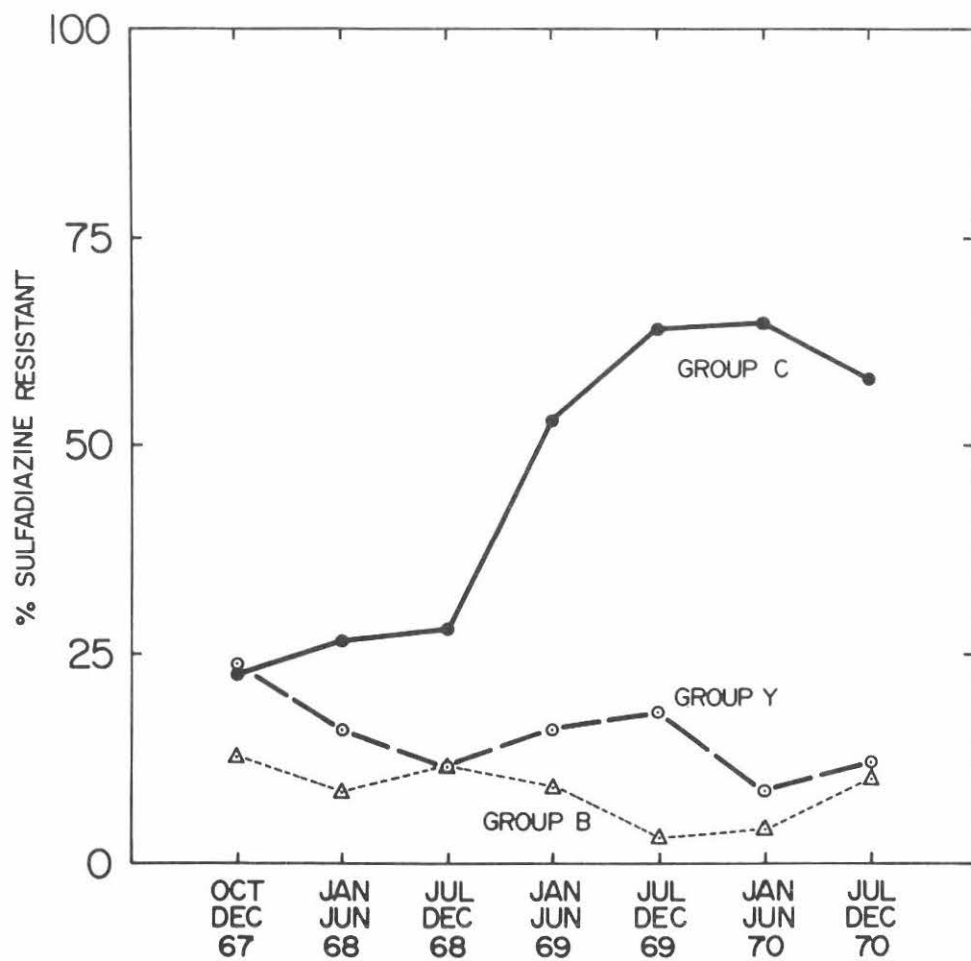


Fig. 26. Sulfa sensitivity patterns of meningococcal isolates from men reporting for recruit training. Oct 1967 - Dec 1970.

Table V. Meningococcal Serogroups Isolated from Naval Personnel,
Great Lakes, June 1967 - May 1970

<u>Serogroup</u>	<u>Number</u>	Positive cultures	
		<u>Percent</u>	
Y	10,796	51	
Agglutinates ≥ 2 antisera	3,457	16	
C	3,007	14	
B	2,261	11	
Autoagglutinable	811	4	
29E	248	1	
Non-typeable	356	2	
Z	109	< 1	
X	66	< 1	
135	27	< 1	
A	9	< 1	
Total positive cultures	21,146		
Total, all cultures	47,933		
Percent positive	44%		

Table VI. Percent Meningococcal Serogroups, Naval Personnel, Great Lakes

<u>Personnel status</u>	June 1967 - May 1969			Period Serogroup	June 1969 - May 1970		
	<u>B</u>	<u>C</u>	<u>Y</u>		<u>B</u>	<u>C</u>	<u>Y</u>
Recruits							
Upon arrival from civilian life	6	2	4		4	2	4
After nine weeks training							
Receiving sulfadiazine	2	8	40		1	7	33
In surveillance companies, no sulfadiazine	4	9	41		1	6	29
Service School							
Arriving from other Naval activities	9	6	6		5	9	12

Table VII. Percent Meningococcal Carriers, Naval Personnel, Great Lakes

<u>Personnel status</u>	<u>Period</u>	
	<u>June 1967 - May 1969</u>	<u>June 1969 - May 1970</u>
Recruits		
Upon arrival from civilian life	22	20
After nine week training		
Receiving sulfadiazine	58	51
In surveillance companies, receiving no sulfadiazine	65	51
Service School		
Arriving from other Naval activities	43	38

Table VIII. Sulfadiazine Resistance Patterns* of N. meningitidis Isolates from Men Reporting for Recruit Training, Great Lakes, Oct 1967 - Dec 1970

<u>Serogroup</u>	<u>1967 Oct-Dec</u>	<u>1968 Jan-Jun</u>	<u>1968 Jul-Dec</u>	<u>1969 Jan-Jun</u>	<u>1969 Jul-Dec</u>	<u>1970 Jan-Jun</u>	<u>1970 Jul-Dec</u>
B	12.5%	8.3%	11.0%	9.1%	3.2%	4.1%	10.0%
C	22.2	26.0	27.8	52.5	54.0	64.5	57.8
Y	23.3	15.4	11.2	15.3	17.8	8.8	11.6
RAS	NT	5.5	5.6	9.1	8.6	13.4	10.0
Other	0	3.5	5.3	7.7	7.8	11.4	8.3
All types	10.5	11.3	9.1	12.6	12.8	14.9	12.8
Total number of samples	1,644	3,299	3,076	2,944	2,952	3,372	3,497

*Resistant to 1 mg sulfadiazine

meningitidis on their initial nasopharyngeal (NP) cultures. Blood sera and NP cultures were collected at approximately weekly intervals until the company was graduated. The correlation between meningococcal isolations and 4-fold or greater increase in antibody titer is shown in Figure 27. The majority (75 percent) of the "susceptible" recruits became carriers by the 40th day of training (Fig. 27 and 28). The lag between the first positive culture and a 4-fold or greater CF response averaged 9 days. Only 2 men failed to respond serologically to meningococci during training. One of these men was not shown to be a carrier until day 63 and may not have had time to produce significant antibody before the final blood specimen was obtained on day 71. It is evident from this study that meningococci can spread rapidly in a recruit company, and that carrier status is followed by a significant antibody response.

The rapidity, magnitude and duration of the antibody response to meningococcal infections (carrier) appear in Figure 29. The antibody response reaches its peak between 14 and 28 days after acquisition of meningococci. The titer remains elevated until about the 59th day and gradually returns to a level only slightly higher than the original. The gradual reduction in antibody titer occurs while one maintains the carrier status. Antibody produced in response to nasopharyngeal acquisition of meningococci does not eliminate the carrier status. Post-infection sera from recruits used in the mouse protection test provides protection against many LD₅₀'s of meningococci. This suggests that antibody protects against meningococcal disease, though its presence fails to eliminate the carrier state.

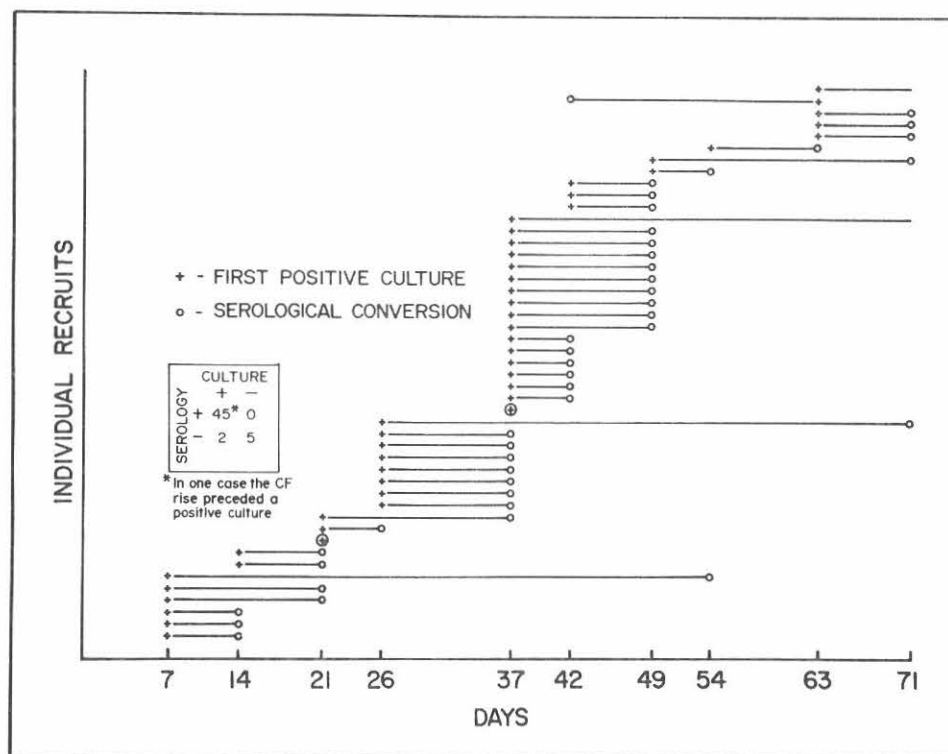


Fig. 27. Distribution and time of acquisition of meningococcal infections in 52 navy recruits.

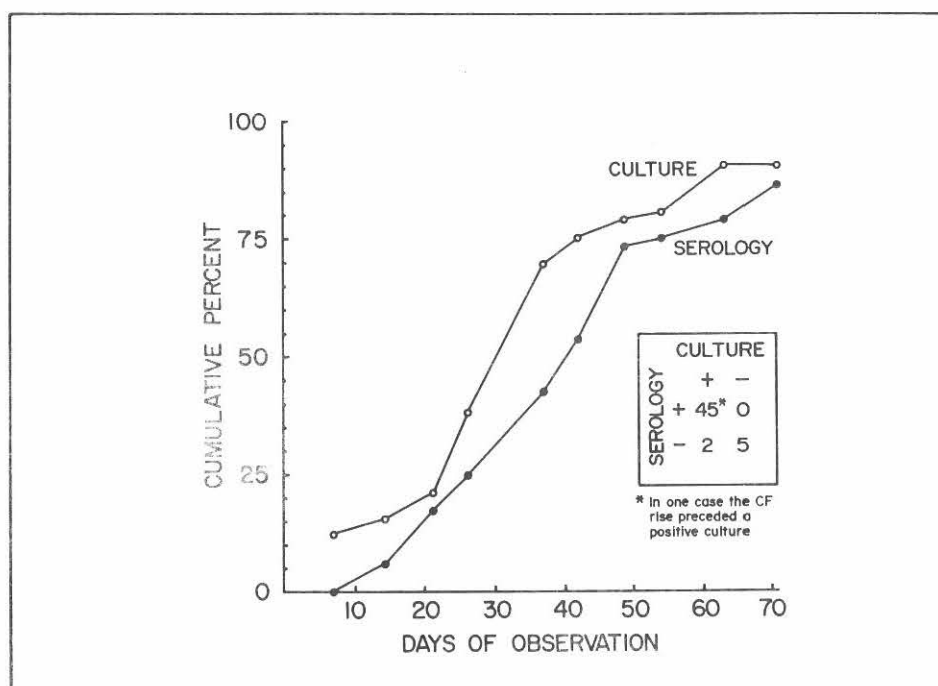


Fig. 28. Comparison of cumulative percentage of meningococcal acquisitions and CF serological conversions during training.

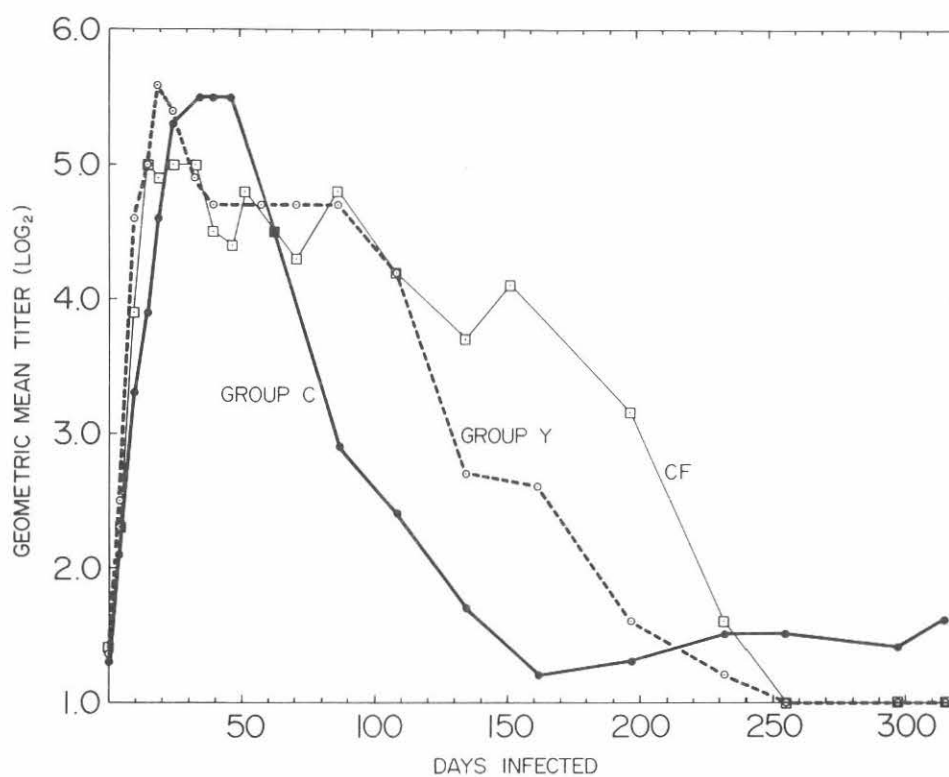


Fig. 29. Serological response to meningococcal infections.

SUMMARY

A longitudinal study of microbial agents or serological evidence of infections causing acute respiratory or meningococcal disease in recruits at Great Lakes has been in progress since 1964. This study provides information on the incidence of infection; seasonal patterns of infection; clinical and subclinical infections; and hospital admission rates caused by various infectious agents operating in the recruit population.

The major etiological agents associated with ARD were adenovirus, types 4 and 7, the former virus type being predominant. In general, adenovirus infections tended to be associated with the severe forms of ARD, especially those in which fever was present.

Influenza virus infections, while present in considerable numbers serologically, was not associated with excessive ARD admission rates. Influenza A2 infection tended to occur during the months of November and December with lower incidence at other times of the year. Influenza B infections were observed sporadically with less incidence than in influenza A2.

Rhinovirus infections appear to be endemic in these populations and are associated with the milder forms of ARD or common cold. While only 9 percent of the men sampled were free of antibody to the rubella virus, more than 70 percent of these became infected during recruit training. During the winter season (November through March) more than 95 percent of those recruits reporting without antibody to rubella subsequently showed seroconversions.

M. pneumoniae infection rates were highest during the late summer season. It is clearly evident from this longitudinal surveillance that pneumonia associated with M. pneumoniae infections are a discrete clinical entity with no relationship to ARD.

The routine Bicillin prophylaxis program instituted in 1961 has virtually eliminated streptococcal infections and rheumatic fever sequela from this population. Streptococcal infection rates were less than 10 percent.

Finally, meningococcal infections and disease have become a serious problem because of the organism's increase in resistance to sulfadiazine.

Sensitivity patterns of N. meningitidis group C isolations from incoming recruits has markedly changed from 1967 to 1970 (80 percent sensitive in 1967 to only 33 percent in 1970). N. meningitidis group C has occurred seasonally (January through May) and has been the predominant group associated with meningococcal disease. This is in contrast to N. meningitidis group B isolations in that more than 90 percent of the isolates of this group from incoming recruits were sulfa sensitive. There has not been a case of meningococcal disease caused by group B since 1967. Slightly over 20 percent of the men reporting for recruit training were carriers of various groups of N. meningitidis, while between 30 to 40 percent of the "seasoned" personnel reporting to service school were found to be carriers. Laboratory data showed that as many as 80 percent of the recruits became carriers by the end of the recruit training. N. meningitidis group Y has been the predominant organism found in recruits upon completion of training.

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13. ABSTRACT A longitudinal surveillance program for microbial infections associated with ARD in recruits during recruit training at Great Lakes has been carried out since 1964. Adenovirus type 4 has been the predominant agent associated with severe ARD infection. Influenza A2 has occurred seasonally but was not associated with an increase in ARD admissions. Rhinovirus infections were associated with the milder ARD complaints. Ninety-one percent of the men had rubella antibody upon arrival for recruit training. In spite of this; over 70 percent of those without antibody seroconverted. <u>N. meningitidis</u> infections were as high as 80 percent by the end of recruit training. <u>N. meningitidis</u> group Y has been the predominant group identified since 1964. <u>N. meningitidis</u> group C made its first appearance in January 1968 and has occurred seasonally (winter - late winter) since. Group C has been the dominant group associated with meningococcal disease. Streptococcal infections have not been a serious problem since the institution of routine penicillin prophylaxis.		

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14. KEY WORDS	LINK A		LINK B		LINK C	
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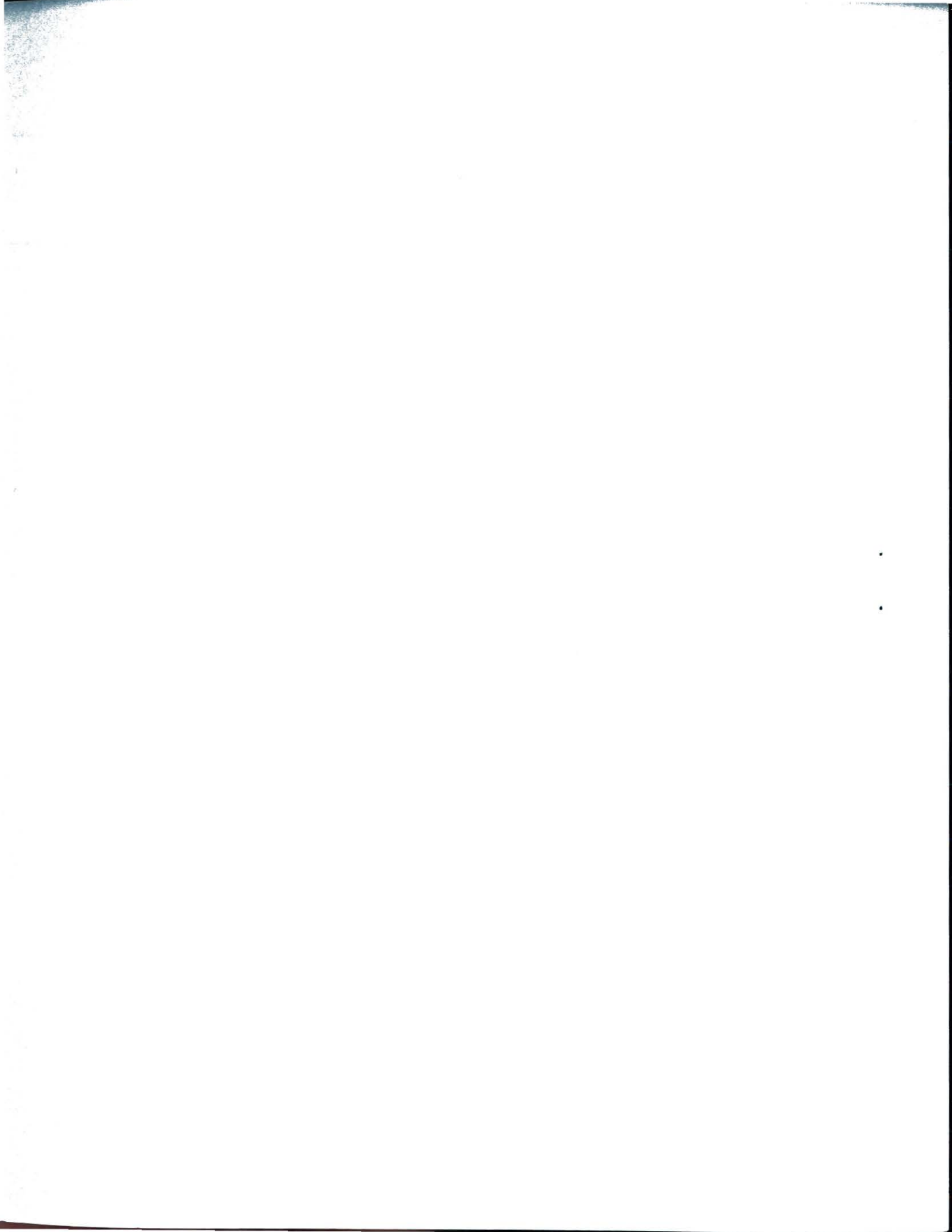
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